Effects of Cognitive and Physical Enrichment on Measures of Autobiographical Memory and Theory of Mind in non-MCI Parkinson's Patients

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Abbreviations

ABM	Autobiographical memory
AD	Alzheimer's disease
ADAS-Cog	Alzheimer's Dementia Assessment Scale-Cognitive
AI	Autobiographical Interview
AMI	Autobiographical Memory Interview
BDS	Blessed Dementia Scale
BVMT	Brief Visuospatial Memory Test
CVLT	California Verbal Learning Test
D-KEFS	Delis-Kaplan Executive Function System
DMN	Default Mode Network
dmPFC	Dorsal medial prefrontal cortex
DRS	Dementia Rating Scale
EAMI	Episodic autobiographical memory interview
FMRI	Functional magnetic resonance imaging
FPR	Faux Pas Recognition
GDS	Geriatric Depression Scale
HADS	Hospital Anxiety and Depression Scale
HC	Healthy controls
HDEC	Health Disability Ethics Committee
HRC	Health Research Council
H&Y	Hoehn & Yahr Clinical Staging
MCI	Mild cognitive impairment
MDRS	Mattis Dementia Rating Scale
MMSE	Mini-Mental Status Exam

MoCA	Montreal Cognitive Assessment
mPFC	Medial prefrontal cortex
MTA	Motor Transport Alliance
MTL	Medial temporal lobe
NPD	Neuropsychological Parkinson's disease
NZBRI	New Zealand Brain Research Institute
PCC	Posterior cingulate cortex
PD	Parkinson's disease
PD-D	Parkinson's disease with Dementia
PD-MCI	Parkinson's disease with mild cognitive impairment
PFC	Prefrontal cortex
PSTS	Posterior superior temporal sulci
REM	Rapid eye movement
RME	Reading the Mind in the Eyes
SDMT	Symbol Digit Modality Test
SLB	Sydney Language Battery
SNc	Substantia nigra pars compacta
TEA	Test of Everyday Attention
TMT	Trail Making Test
ToM	Theory of Mind
TPJ	Temporo-parietal junction
UPDRS	Unified Parkinson's disease Rating Scale
VOSP	Visual Object and Space Perception

Abstract

The current study investigated the effects of an eight-month randomized controlled trial, comprising combined physical and cognitive enrichment, on measures of personal autobiographical memory (ABM) and theory of mind (ToM) in idiopathic Parkinson's disease (PD). These patients had a non-MCI status. Research suggests that ToM and ABM may be impaired early in PD, prior to the emergence of other cognitive deficits. PD participants were randomised to an active intervention group (*n*=21) or passive control group (usual care plus frequent researcher contact; *n*=19), and performance at baseline and end-of-trial was compared with an age, education and sex-matched healthy control group (HC; *n*=24). A combination of the Autobiographical Memory Interview (AMI) and Episodic Autobiographical Memory Interview (EAMI) was used to assess semantic and episodic memory, with a particular focus on the examination of sensory-perceptual and contextual detail associated with autonoetic episodic recall. A card sequencing False Belief story task assessed cognitive ToM. Overall, PD participants showed significantly impaired performance on both AMI and EAMI measures of episodic memory; for semantic memory, the PD group had poorer recall on the AMI, but this difference only emerged for later adulthood and especially recent memory for the EAMI measure at end-of-trial. For ToM, a significant pre-post RCT interaction effect was found due to a low mean ToM score in the PD intervention group that increased to a similar mean score of both the HC and PD-passive groups at end-of-trial. However, no other effect of intervention was found in the non-MCI PD participants. Although the sample size was relatively small, this study suggests that a relatively intensive combination of cognitive and physical exercises does not benefit PD participants prior to an MCI status. Further follow up is required to test whether intervention effects emerge over the longer term.

Chapter 1: Introduction

1.1 Parkinson's disease

Idiopathic Parkinson's disease (PD) is a progressive multisystem neurodegenerative disorder that currently affects approximately 10,000 New Zealanders (Myall et al., 2016). With age as its single most significant risk factor (Hindle, 2010), the incidence rate of PD in New Zealand is increasing as the population grows older. The cardinal motor symptoms of PD are bradykinesia, rigidity, slow and rhythmic resting tremor, and postural instability (Halliday & McCann, 2009). These symptoms provide its differential diagnosis. However, the debilitation associated with PD goes beyond motor impairment to include a broad and heterogeneous spectrum of non-motor symptoms, some of which antedate diagnosis and all of which become more prevalent as PD progresses (Aarsland, Andersen, Larsen, & Lolk, 2003; Jellinger, 2011). This can include disruption to autonomic and sensory functions, the sleep-wake cycle, rapid eye movement sleep, and neuropsychiatric symptoms (Lim, Fox, & Lang, 2009; Poewe, 2008). Many patients experience depression, sensory pain, hyposmia, orthostatic hypotension, constipation, incontinence and genital dysfunction (Poewe, 2008). Falls, abnormal sweating, dysphagia, dribbling, vivid dreams and restless legs, experiences of apathy, anhedonia and hallucinosis are also part of the diverse symptomatic profile of PD (Hindle, 2010; Jellinger, 2011; Poewe, 2008). For many, among the most distressing and disabling of PD symptoms is the experience of progressive cognitive decline, which often has a more severe impact on quality of life than its motor symptoms. Although time courses are highly variable, dementia (PDD) within 20 years is the prognosis for 80% of PD patients (Aarsland et al., 2003; Buter et al., 2008; Hely, Reid, Adena, Halliday, & Morris, 2008; Wood et al., 2016).

The neuropathological underpinnings of PD symptoms primarily involve the gradual deposition perhaps over many decades, of abnormal aggregations of misfolded alpha-synuclein proteins, known as Lewy bodies and neurites, in the brain. These result in synaptic and cellular loss. Alzheimer's related beta-amyloid and hyper-phosphorylated tau pathology is also suggested to be a contributing factor (Jellinger, 2011). Over time, a cascade of disruptions to cortico-striato-thalamocortical and cortico-cortical circuitry (Jellinger, 2011), caused by diffusion of Lewy pathology, affect multiple systems and give rise to the plethora of symptoms seen in PD. The Braak staging model (Figure 1.1), depicts Lewy pathology as spreading predictably from the anterior olfactory nucleus through the midbrain and across the neocortex (Hawkes, Del Tredici, & Braak, 2010; Hindle, 2010; Zapiec et al., 2017). The pathology is more prevalent in neurons with long, thin and poorly myelinated axons (Braak, Ghebremedhin, Rüb, Bratzke, & Del Tredici, 2004). These features include the dopaminergic striatal projection neurons in the substantia nigra pars compacta (SNc). The degeneration of these cells are the primary cause of PD motor symptoms, as the loss of this neurotransmitter in the striatum affects dopamine-dependent priming of neurons associated with incoming neocortical messages (Curtis, 2018). Cognitive deficits and dementia are associated with Lewy-induced cellular and synaptic degeneration primarily in many structures including brain stem nuclei, limbic structures and cerebral cortex. There is also reduced cortical cholinergic activity and dysregulation of catecholamine and serotonergic neurotransmitter systems.

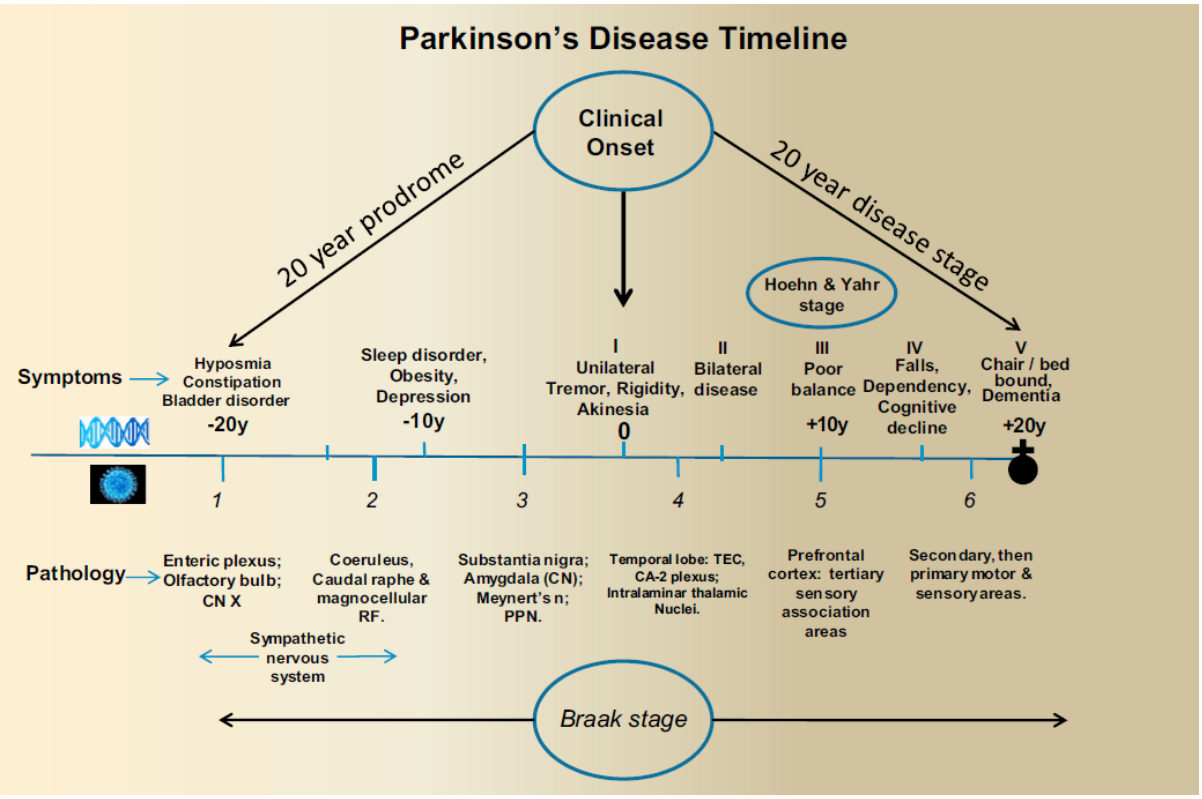


Figure 1.1: Braak staging of spread of pathology, from symptom onset to end of disease course. Pathological staging is indicated by 1 – 6 numbering. Prodromal symptoms are indicated to the left of clinical onset, with major features based on Hoehhn & Yahr staging to the right. The extreme left hand side symbols represent possible causative agents of genetic mutation (upper) or viral infection: *Abbreviations*: CA2 = Ammon's horn second section; CN X = cranial nerve motor component; RF = reticular formation; CN amygdala central subnucleus; Meynert's n = basal nucleus of Meynert; PPN = pedunculopontine tegmental nucleus; TEC = transentorhinal cortex. *Reprinted with permission of Hawkes et al. (2010).*

1.2 Parkinson's disease and cognitive impairment

The profile of cognitive impairment in PD is characterized by slow and non-insidious decline across one or more cognitive domains including attention, executive function, visuospatial function, memory and language. Factors associated with progression to dementia include older age of disease onset, greater severity of motor symptoms, longer disease duration and advanced disease stage (Aarsland & Kurz, 2010; Wood et al., 2016). About 25-30% of non-demented Parkinson's patients have PD-MCI (Litvan et al., 2011; Wood et al., 2016). PD-MCI can be defined as a state of cognitive performance that is lower than expected for an

individual's age and level of education, but which is not severe enough to interfere with activities of everyday living (Ritchie, 2004). Although dementia is not a predetermined outcome and some PD-MCI patients may even improve, PD-MCI patients have a high risk of conversion when compared with cognitively unimpaired PD patients (Goldman, Aggarwal, & Schroeder, 2015; Wood et al., 2016).

Neuroimaging evidence has also shown that some cognitively unimpaired individuals with PD show physical alterations in the brain prior to any observable cognitive deterioration. This subset is at greater risk of future cognitive decline than those who do not show these volumetric changes (Mak et al., 2015). Additionally, among patients who have presented clinically as cognitively unimpaired but who have gone on to develop MCI within four years, a discrete risk signature has retrospectively been identified through lower z scores across selected neuropsychological tests (Myall et al., 2015). Given this neuroimaging and cognitive evidence that a tangible stage of risk can be identified before any overt indications of cognitive decline, there is clearly a degree of risk even prior to a PD-MCI diagnosis in some patients. Thus PD with pre-MCI risk may be a suitable identifier of the cognitively vulnerable patients, and represents a critical time window for early interventions that aim to slow or prevent its further progression.

Unlike the responsiveness of motor symptoms to dopamine replacement therapy, many cognitive symptoms in PD persist despite optimal medical management. There is little by way of pharmacologic therapy that can support preservation of cognitive function (Bloem, de Vries, & Ebersbach, 2015; Lim et al., 2009). Instead, research literature suggests that possible ways to slow cognitive decline include taking regular exercise. This may maintain healthy blood supply to the brain (Hahn & Andel, 2011), as well as encourage cognitive and social stimulation. There is substantial interest in nonpharmacological, 'lifestyle' interventions that may slow progression of cognitive impairment in PD. In the AD field, there

is already evidence that cognitive and physical activity is associated with a reduced risk for cognitive decline (Hindle, Petrelli, Clare, & Kalbe, 2013). Initial trials of aerobic exercise in PD have produced evidence of cognitive improvement (Hindle et al., 2015). It has therefore been suggested that promotion of brain resilience through exercise or cognition-focused interventions, may help to delay or even prevent the onset and later progression of impairment in PD (Hindle et al., 2013). However, there is currently insufficient evidence regarding the benefits of such interventions in PD and a lack of well-controlled studies (Heyn, Abreu, & Ottenbacher, 2004; Hindle et al., 2013; Lautenschlager, Cox, Flicker, & et al., 2008). The current PD Enrichment Study was designed to establish preliminary evidence, through a randomized controlled trial, of whether an extended non-pharmacological treatment regime comprising weekly cognitive and physical exercises would help to maintain cognition and motor function in PD. The current study was conducted with a participant group of well-characterized early-stage pre-MCI PD patients assessed as cognitively normal and assessed risk of progression to MCI. The intervention package included cognitive tasks that aimed to activate neural regions associated with the default mode network (DMN) as well as other large scale cognitive brain networks. The DMN is notable in supporting autobiographical memory and theory of mind processes. The aim of the current thesis project was to therefore examine the effects of intervention on performance in measures of autobiographical memory and theory of mind within this cohort and a group of matched HC participants.

1.3 The Default Mode Network

The default mode network (DMN) refers to an interconnected and anatomically defined network of brain regions that are metabolically active when the brain is at rest and engaged in internally-directed modes of thought. It becomes relatively deactivated when attention is focused on externally-directed tasks of the immediate present, which activate other large neural networks (Andrews-Hanna, 2012; Buckner, Andrews-Hanna, & Schacter, 2008;

Gusnard & Raichle, 2001; Minoshima et al., 2004). The evolutionary adaptive utility of the DMN appears to include using past experiences to anticipate and prepare for the future and alterative scenarios, as well as facilitating successful social interactions and cooperation as a group-oriented species (Tessitore et al., 2012).

Activation of the DMN, as observed in fMRI, occurs when the mind's attention shifts from the immediate present and engages in a broad range of personally and motivationally salient social, emotional and mnemonic processes. These processes include recollection of episodic autobiographical information from the past, as well as prospection of contextually realistic future events (Andrews-Hanna, 2012; Andrews-Hanna, Reidler, Huang, & Buckner, 2010; Buckner & Carroll, 2007; Schacter, Addis, & Buckner, 2008; Spreng & Grady, 2009; Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010; Tessitore et al., 2012). This 'awareness of one's protracted existence across subjective time' (Buckner & Carroll, 2007, p. 50), is referred to as autonoetic consciousness in autobiographical memory research. It is characterized by rich contextual detail across several sensory-perceptual modalities (Buckner & Carroll, 2007; Irish, Lawlor, O'Mara, & Coen, 2008; Tulving, 1985). Regions of the DMN are also activated when conceiving the thoughts and feelings of oneself and others, as well as during some forms of topographical or spatial navigation (Buckner et al., 2008; Buckner & Carroll, 2007).

A model presented by Andrews-Hanna (2012; Figure 1.2), portrays the DMN as a collection of subsystems and hubs, in which the dorsomedial PFC (dMPFC) subsystem and medial temporal lobe (MTL) subsystem serve social cognitive and recollection-based operations respectively. These two subsystems converge on core hubs within the posterior cingulate cortex (PCC) and medial prefrontal cortex (mPFC), which appear important to the overall integration of the subsystems network. The MTL subsystem comprises the MTL, retrosplenial cortex, posterior cingulate cortex, posterior inferior parietal lobe and mPFC

regions, as well as the hippocampus and parahippocampus (Buckner et al., 2008; Cabeza & St Jacques, 2007; Spreng & Grady, 2009; Svoboda, McKinnon, & Levine, 2006). The dorsal medial subsystem recruits the dmPFC, precuneus, mPFC, temporoparietal junction, lateral temporal cortex and temporal poles (Frith & Frith, 2003; Tessitore et al., 2012).

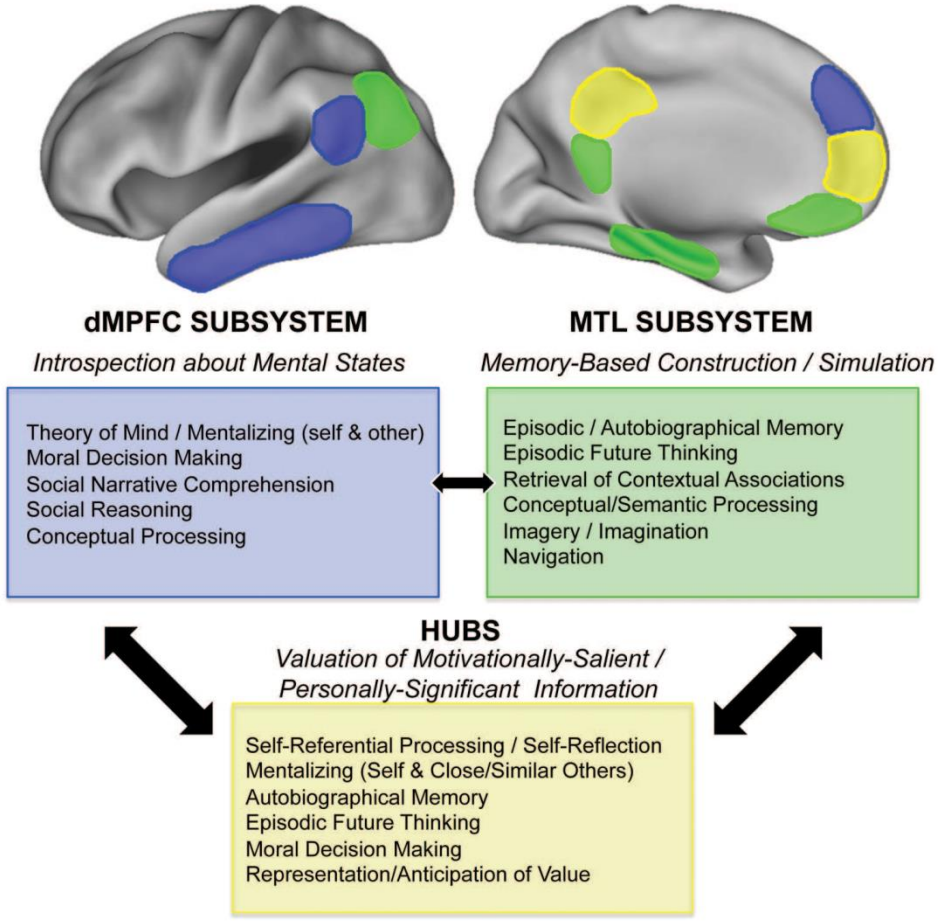


Figure 1.2: Proposed functional-anatomic organization of the major subsystems and hubs of the default mode network. Arrows represent approximate strength of connectivity between components. *Reprinted with permission from Andrews-Hanna (2012).*

Studies of age-related disruption to the DMN and the other large-scale brain networks indicate that a degradation of network connectivity is a natural part of the ageing process (Andrews-Hanna et al., 2007). However, in individuals with PD, there may be advanced reduction in functional integrity of the DMN that may in particular contribute to development of early cognitive impairment. In early stage (H&Y 1-2; Goetz et al., 2004), cognitively

unimpaired PD patients (as defined by z scores that do not fall below the population mean in any three cognitive domains), neuroimaging data has shown functional disruption of the DMN to occur in the right medial temporal lobe and bilateral inferior parietal cortices, in the absence of significant structural differences, compared with controls (Tessitore et al., 2012). Similar DMN-associated hypometabolic patterns have been observed in cognitively unimpaired non-PD patients who carry a genetic loading for Alzheimer's disease (Buckner et al., 2008). Overall, there is evidence to support the possibility that the DMN is vulnerable to disturbance even prior to emergence of cognitive or structural deficits in PD. This carries important implications for therapeutic interventions that seek to foster brain resilience in the very earliest clinical stages of PD, and efforts to slow progression to PD-MCI and PDD.

1.4 Theory of Mind

Theory of Mind (ToM) is a complex domain of social cognition referring to the ability to infer emotional and mental states of others, in order to understand and predict their behaviour. Interpreting other people's emotions, beliefs, intentions and desires enables the forming and maintenance of social bonds and successful daily interactions (Bodden et al., 2010). Deficits in these abilities can go on to severely impact social engagement and quality of life.

Neuroimaging research over the last decade has identified the existence of a distributed neural network underpinning ToM abilities. Regions of this network include the posterior superior temporal sulci (pSTS), temporo-parietal junctions (TPJ), precuneus, posterior cingulate cortex and the prefrontal cortex (PFC; Poletti, Enrici, & Adenzato, 2012). Particular emphasis is made of the contribution of the prefrontal and frontal brain regions to cognitive and affective subcomponents of ToM (Poletti et al., 2012; Roca et al., 2010). Cognitive ToM can be understood as the ability to infer other people's beliefs, intentions and

desires. Affective ToM refers to the ability to infer and empathize with other people's emotional states and feelings (Nobis et al., 2017).

A model by Shamay-Tsoory and colleagues (2005; cited by Poletti et al. (2012) proposes that cognitive and affective sub-processes of ToM operate within separate systems mostly housed within the PFC, with more posterior brain regions involved in background operations (see Figure 1.3). In this model, the ventromedial PFC is recruited to affective ToM, and the dorsolateral PFC to cognitive ToM. Although frontal-lobe underpinnings of affective ToM are well-established by lesion and neuroimaging evidence (Bodden et al., 2010), the regions supporting cognitive ToM are not clearly elucidated. Key evidence for the role of the dorsolateral PFC in cognitive but not affective ToM abilities was shown by Kalbe et al. (2010) using transcranial magnetic stimulation. Additional imaging evidence also indicates a role of the dorsomedial PFC in cognitive-based mentalizing amongst other complex and more abstracted processes (Baetens, Ma, & Van Overwalle, 2017; Bzdok et al., 2012; Molenberghs, Johnson, Henry, & Mattingley, 2016; Schurz, Radua, Aichhorn, Richlan, & Perner, 2014).

Regions of overlap between ToM and DMN processes include the dorsal and ventral medial prefrontal cortices, posterior cingulate cortex, precuneus and temporo-parietal junctions (Andrews-Hanna, 2012; Spreng & Grady, 2009). Whilst the ventromedial PFC forms a node of the DMN, the dorsolateral prefrontal cortex is more strongly associated with the central executive brain network. However, this network is also a target for cognitive stimulation in the PD Enrichment study. Characterized behaviourally by symptoms of executive dysfunction, the central executive network also shows abnormal fMRI activity in early-stage PD (Sala et al., 2017).

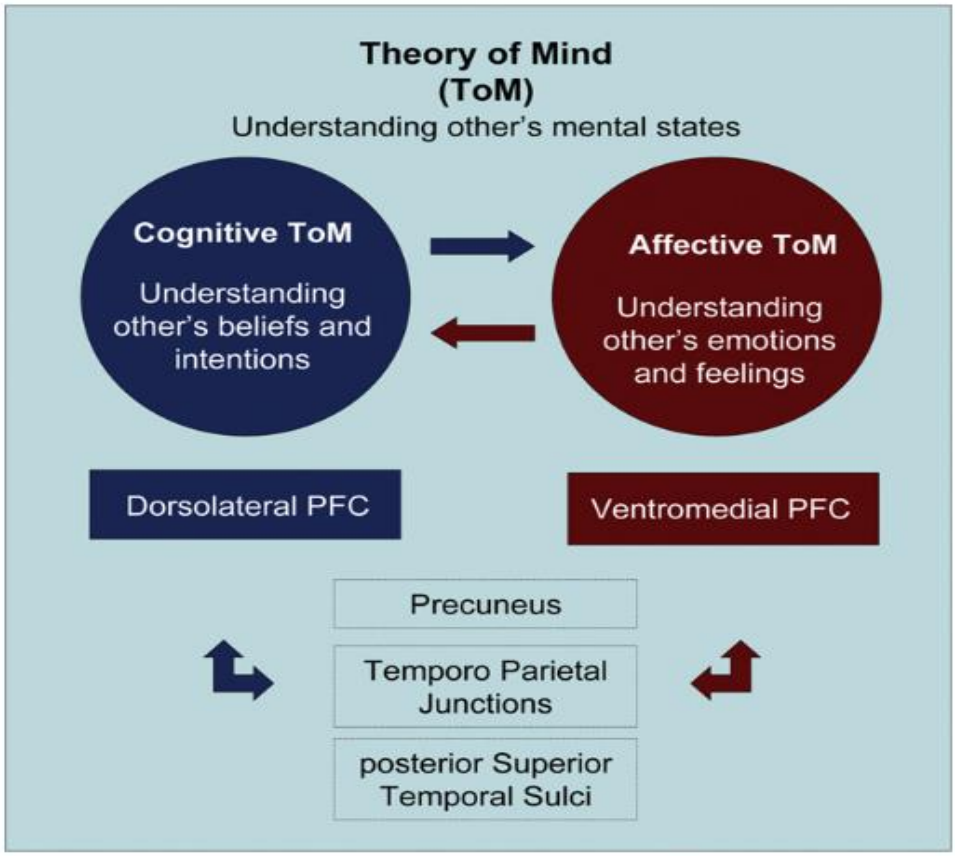


Figure 1.3: A frontal lobe model of the relationship between two neural systems for cognitive and affective ToM processing, with supporting posterior regions. *Reprinted with permission of Poletti et al. (2012).*

1.4.1 Theory of Mind in Parkinson's disease: literature review

The discovery of affective and cognitive subcomponents of ToM was facilitated by the development of several types of tests that sought to examine people's beliefs about other's beliefs, about other's feelings, or both (Poletti et al., 2012), across different clinical populations and in normal human development. The following literature review describes four of the most commonly used tests used in studies published between 2000 and 2010 to evaluate the neuropsychological features of ToM impairment in non-demented PD patients, screened by a range of cognitive measures (Table 1-1). References to Hoehn & Yahr clinical staging is based on recommendations made by the Movement Disorder Society Task Force

(Goetz et al., 2004; Poletti et al., 2012), which defines early H&Y stages as 1, 1.5 and 2; moderate as 2, 2.5 and 3; and advanced as H&Y stages 4 and 5.

Reading the Mind in the Eyes (RME) task is a measure of affective ToM abilities. This task was one of the cognitive exercises in the current PD Enrichment study, which sought to examine whether a non-pharmacological treatment regime comprising weekly cognitive and physical exercises would help to maintain cognition in PD. In the RME task, participants are typically presented with 27-36 images of human eye regions and must name which of several basic emotions the eyes are conveying (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Poletti et al., 2012). Of six studies that used the RME task in PD patients, four reported preserved performances in medicated PD patients up to moderate clinical stages (H&Y2.5) and mean disease duration of 10.2 years (Euteneuer et al., 2009; Péron et al., 2010; Péron et al., 2009; Roca et al., 2010). Another two studies reported impaired performance (Bodden et al., 2010; Mimura, Oeda, & Kawamura, 2006) in non-demented PD patients screened with the Mini Mental State Examination (MMSE cutoff >26; Folstein, Folstein, & McHugh, 1975) and Parkinson Neuropsychometric Dementia Assessment (PANDA; Kalbe et al., 2008). However, Mimura & colleagues (2006) noted that both PD and HC scored relatively highly overall. In the study by Bodden et al., (2010), the younger age of the HC compared to PDs (mean age 58.7years, versus 63.7 years respectively) may have been an influencing factor as RME performance appear to decline even in healthy ageing (Pardini & Nichelli, 2009). Additionally, a similar mean performance to Bodden et al. (2010) was reported by (Euteneuer et al., 2009) which found no significant difference in performance of PD patients compared to HC. Overall, the RME task indicates that affective ToM abilities may be preserved in PD, up to ten years beyond diagnosis.

Table 1-1. *Characteristics of theory of mind in Parkinson's disease studies. The order is chronological.*

Author(s)	Sample	Disease Duration in Years (SD), Hoehn & Yahr Staging	Patients' Mean Age in Years (SD)	Cognitive Measures	ToM Tasks	ToM Component	Main Results
Saltzman et al., 2000	11 PD non-demented 8 HC	Duration - not reported H&Y - 2.5	71 (13.45)	MMSE (cut-off > 26), Vocab subtest of WAIS-R, CCST, Verbal Fluency Task, Five-Point Fluency Task	False Belief Perspective taking Deception task	Cognitive Cognitive Cognitive	Impaired Preserved Preserved
Mengelberg & Siegert, 2003	13 PD non-demented 11 HC	Duration - 5.4 H&Y II - 4, III - 6 III, IV - 2	72.9 (8.9)	MMSE (cut-off > 26), NART	Visual False Belief Short Passage Task First Order Short Story Second Order Short Story	Cognitive Cognitive Cognitive Cognitive	Impaired Impaired Impaired Preserved
Mimura et al., 2006	18 PD non-demented 20 HC	Duration - not reported H&Y - 2.5	68.9 (7.0)	MMSE (cutoff > 26), WCST, Stroop, Mazes, Verbal Fluency	RME	Affective	Impaired
Kawamura & Koyama, 2007	11 PD non-demented 20 HC	Not reported	67.1	MMSE (28.1, 2.6)	FPR	Cognitive Affective	Impaired Preserved
Euteneuer et al., 2009	21 PD non-demented 23 HC	Duration - 7.1 (6.0) H&Y - 2.5 UPDRS-3 - 17.7	67.6 (7.3)	MMSE (140.3, 2.9), DemTect, LPS, MCST, Verbal Fluency (FAS and animals), Subtest 4 of German Intelligence Test battery	RME	Affective	No difference / Preserved
Peron et al., 2009	17 Early PD on & off meds 26 HC 27 Advanced PD non-demented 26 HC	Duration Early - 2.5 (1.5); H&Y - 1.5 (on) / 1.5 (off) Duration Advanced - 10.2 (4.9); H&Y - 1.3 (on) / 2.5 (off)	61.0 (7.1) 56.6 (7.8)	MDRS (score > 130), MCST, TMT, Categorical/Literal Fluency, Stroop	RME FPR RME FPR	Affective Cognitive & Affective Affective Cognitive & Affective	Preserved (on & off) Both Preserved (on & off) Preserved (on & off) Impaired Cognitive
Bodden et al., 2010	21PD non-demented 21HC	Duration - 5.1 (2.8); H&Y - 2.5 (Range 1 - 3)	63.7 (10.0)	MMSE (29, range 28-30), MDRS, PANDA, Verbal Memory, Digit Span, Letter & Semantic Fluency, TMT, Reasoning Task	RME	Affective	Impaired
Peron et al., 2010	13 PD non-demented 13HC	Duration - 10.5 (3.6); H&Y - 1-2	53.3 (8.5)	MDRS (score > 130), MCST, TMT, Categorical/Literal Fluency, Action (verb) Fluency, Stroop	RME	Affective	Preserved
Roca et al., 2010	36 PD non-demented (incl. 20 non-medicated) 35 HC	Duration Medicated - 1.69 (1.55); H&Y - 1.42 (0.57) Duration Unmedicated - 1.23 (1.56); H&Y - 1.33 (0.54)	Medicated 63.4 (8.47) Unmedicated 63.5 (11.5)	MMSE (Medicated 29.00, 1.55 / Unmedicated 28.26, 1.45), Categorical/Phonologic Verbal Fluency, Boston Naming, Token Test, Rey Auditory Verbal Learning Test, Delayed Recal Complex Rey Figure & Attention, TMT, Digit Span, WCST	RME FPR RME FPR	Affective Cognitive & Affective Affective Cognitive & Affective	Preserved Impaired Cognitive Preserved Impaired Cognitive

Abbreviations: CCST = California Card Sorting Task; FPR = Faux Pas Recognition; H&Y = Hoehn & Yahr; HC = Healthy Controls; LPS = Leistungsprufsystem; MDRS = Matis Dementia Rating Scale; MMSE = Mini-Mental Status Exam; NART = National Adult Reading Test; PANDA = Parkinson Neuropsychometric Dementia Assessment; PD = Parkinson's Disease; RME = Reading the Mind in the Eyes; TMT = Trail Making Test; WAIS-R = Wechsler Adult Intelligence Scale - Revised; WCST = Wisconsin Card Sorting Test. Table adapted from Poletti, Enrici, Bonuccelli & Adenzato, 2011; Bora et al., 2015.

Another type of ToM task is the Faux Pas Recognition task, which was also included in the cognitive stimulation package of the PD Enrichment study (see Appendix C for an example). This task is a measure of both affective and cognitive ToM abilities, and is often presented as a series of 10-20 cartoon, verbal or written stories which contain either a faux pas or minor conflict which serves as a control condition (Stone, Baron-Cohen, & Knight, 1998). Participants first identify whether anyone said or did anything that would constitute a social transgression, which represents the affective component. They then answer a further set of questions that require inference of the characters' mental states, which represents the cognitive component. All three studies that used this task reported unimpaired performance of early-stage PD patients in the affective component of the FPR task compared with HC (Kawamura & Koyama, 2007; Péron et al., 2009; Roca et al., 2010). For the cognitive aspect, two studies reported impaired performance in early-stage non-MCI PD patients (Kawamura & Koyama, 2007; Roca et al., 2010); whilst another reported emergence of impairment only at more advanced clinical stages (Péron et al., 2009). However, the use of an abridged version of the task in Péron et al. (2009), and not the earlier two, may have influenced the results observed. Overall, findings from studies using the Faux Pas Recognition test suggest the presence of cognitive ToM deficits and preservation of affective ToM in early-stage PD.

The false belief paradigm is also well known in the cognitive ToM literature. First order false belief tasks measure a participant's ability to infer a character's (mistaken) belief about the state of the world, which is different from their own (true) belief (Martins-Junior, Sanvicente-Vieira, Grassi-Oliveira, & Brietzke, 2011). Higher or second-order false belief tasks are more cognitively challenging and typically require the participant to infer what one character believes another to character to (falsely) believe (Baron-Cohen, Leslie, & Frith, 1985; Poletti et al., 2012). Adult versions of the task usually involve reading or listening to a story and then answering test question verbally.

Two studies reported impaired first order performance in early stage PD patients (Mengelberg & Siegert, 2003; Saltzman et al., 2000). However, one of these studies also employed a deception task and perspective-taking task. These tasks involve for example, detecting deception in an examiner's actions to correctly guess the eggcup under which a paper clip is hidden. Another is showing a whole picture, then hiding half of it to create visual ambiguity and requiring a participant to state what they think others might think the picture actually depicts. In both of these latter tasks, the PD group showed preserved performance compared with HC (Mengelberg & Siegert, 2003; Saltzman et al., 2000). However, the heterogeneity inherent to the administration of these tasks meant that variation in cognitive loads not specific to ToM may have been differentially recruited to each study (Saltzman et al., 2000). Indeed, across all types of tests, there is a need to consider variation in attentional and working memory components required of more abstract written and verbal tasks (Brüne, 2005). This is highlighted in the study by Saltzman et al. (2000) which reported an association between ToM and certain measures of executive function (five point verbal fluency); and contrasts with the Faux Pas Recognition results reported by Roca et al. (2010), in which no relationship was found between measures of executive functioning and cognitive ToM. However the earlier association may have actually reflected performance on domain-general processes that support both executive function and ToM, particularly since the false belief task used by Saltzman et al. (2000) controlled for memory problems but not for comprehension and general reasoning abilities.

In recognizing the importance of controlling for non-ToM cognitive loadings, Mengelberg and Siegert (2003) employed a visual false belief card sequencing task in which participants reorganized 18 sets of picture cards into stories that showed a logical sequence of events (Langdon et al., 1997). The task included a false belief condition plus conditions that checked for deficits in sequencing, social understanding and complex reasoning abilities. In

addition to the first order false belief story task (reported earlier), participants also completed second order tasks and read short passages that required inference of mental states or physical causation (Poletti et al., 2012). In the short passage and card sequencing tasks, non-demented PD patients showed significantly poorer ToM performance compared with age-matched HC but spared performance in the conditions that did not measure ToM, suggesting presence of a specific ToM deficit. Both PD and control groups performed comparably on the more challenging second order task, with slightly worse performance in the PD group (p=.09). However, the median score of zero across both groups suggests that the task was simply too hard and possible floor effects may have disguised differences in ability between the two groups (Mengelberg & Siegert, 2003).

Overall, results of these studies suggest that when careful control protocols are place, impairments in cognitive ToM in PD emerge in the earliest clinical stages, and possibly prior to other cognitive impairments. In contrast, the capacity to infer and empathize with other people's emotional states may be preserved ten years beyond diagnosis (Nobis et al., 2017; Péron et al., 2009; Poletti, Enrici, Bonuccelli, & Adenzato, 2011; Roca et al., 2010). This conclusion may be related to the early pathology of PD. The progressive depletion of nigrostriatal dopamine disturbs fronto-thalamo-striatal circuits, which result in hypostimulation of the PFC. In the earliest stages of PD, the spatio-temporal progression of dopamine loss into the striatum is characterized by up to 90% of dopamine depletion in an area of the caudate nucleus engaged in the dorsolateral fronto-striatal circuit. This may be why cognitive ToM and other executive functions are impaired earliest. Affective ToM may be relatively spared until more medial portions of the PFC become destabilized by the cortical dispersion of lewy pathology at later stages (Poletti et al., 2012).

On the basis of neuropsychological and neurobiological evidence that cognitive ToM shows signs of impairment in early-stage PD, a group of 20 well-characterized, at-risk non-

MCI PD patients were assessed on this domain as part of their baseline assessment for inclusion in the current longitudinal study (Nicolson, 2016). Participant overlap occurred because the cohort used in this preliminary work represented the first 20 PD participants recruited to the PD Enrichment trial, which sought to encourage neural reserve in vulnerable PD brain areas at the earliest stage possible. Patients were assessed for cognitive ToM performance using a card sequencing task by Langdon et al. (1997), alongside 15 age and education-matched HC participants who were also included as controls in the current study. This particular task was selected because of its relative prowess in isolating cognitive ToM performance from more general executive-type impairments (Brüne, 2005; Mengelberg & Siegert, 2003). The recruitment of working memory is also minimal in this task compared with others types of measures. In a replication of earlier findings by Mengelberg and Siegert (2003), this preliminary work by Nicolson (2016) showed that PD participants performed significantly worse in the false belief condition compared with HC, even when controlling for the influences of age, sex and education. No differences were found between the two groups in conditions representing more general cognitive abilities. The card sorting task by Langdon et al. (1997) therefore appears to carry utility as a tool for examining the effects of an intervention which is designed to stimulate and support vulnerable PD brain regions that engage the DMN, central executive and other major brain networks.

1.5 Autobiographical memory

Autobiographical memory (ABM) represents the mind's inventory of information and experiences collected over the lifespan. Beyond its utility in navigating the practicalities of everyday life, ABM is important for the construction of personal identity, self-coherence and self-continuity (Piolino, Desgranges, Benali, & Eustache, 2002). The ABM brain network overlaps with the DMN and involves the frontal and medial temporal lobes including the hippocampus and parahippocampus, plus ventral parietal cortices, posterior cingulate cortex

and secondary association areas distributed across the neocortex (Cabeza & St Jacques, 2007). Conceptually, the ABM is distinguished into personal episodic and semantic forms of personal memory. Personal episodic ABM refers to memory for personally-experienced events, with an episodic memory said to contain contextually specific details about an event or incident, including its location in space and time (Piolino et al., 2003; Tulving, 1985, 2001; Tulving, Schacter, McLachlan, & Moscovitch, 1988). Personal semantic ABM refers to the vast knowledge base of facts stored about one's life, which are recalled independently of specific contextual encoding recollections. Examples include birthdates and personal telephone numbers (Tulving et al., 1988). The conceptual distinction between semantic and episodic forms of ABM is represented by hierarchical models in which memory knowledge is held at three levels of abstraction: lifetime periods, general events and event-specific knowledge (Conway & Pleydell-Pearce, 2000; Irish et al., 2011a). Consciousness is inherently engaged as the self, which 'works' these levels in a constant cyclical process of memory encoding and retrieval (Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002). Semantic-based lifetime periods reflect the broadest level of abstraction and comprise general knowledge about distinct themes in a person's life (e.g. schooling, career, later adulthood, and retirement years). These broad time periods provide scaffolding for less abstracted, general events which are grouped as clusters of repeated or thematically related events, such as "first-time" achievements, or playing netball for the school team. These general events in turn are portals to event-specific knowledge, which refers to the detailed visual, emotional and sensory-perceptual representations of an individual episodic event (Levine et al., 2002; Piolino, Desgranges, & Eustache, 2009). The high-fidelity sensory-perceptual episodic details of event specific knowledge tend to fade quickly unless they are part of particularly meaningful events (Conway, 2005). Retrieval of contextual details are also sensitive to the neocortical changes implicated in normal ageing, regardless of remoteness (Levine et al.,

2002). The loss of specificity and detail may be compensated for by expansion of 'general event' semanticised memory stores (Piolino et al., 2006). It is through these more abstract, semantic-based levels of personal memory, that self-knowledge and identity may be preserved over the life course (Levine et al., 2002).

Retrieval of an event with the 'event-specific knowledge' level of contextual detail can often be accompanied by the subjective 're-living' of the original event. This phenomenon is thought to be mediated by autonoetic consciousness, which is associated with regions of the DMN as highlighted previously (Irish et al., 2011a; Irish et al., 2008; Piolino et al., 2002; Piolino et al., 2009). Current research on ABM encourages close examination of the sensory-perceptual contextual details and especially the presence of vivid visual imagery, which is almost always involved in the subjective experience of remembering and is considered to represent a truly episodic memory (Irish et al., 2008; Piolino et al., 2006).

1.5.1 Autobiographical memory in Parkinson's disease: literature review

Research into ABM in normal aging has shown that age-related decline is more pronounced in episodic than semantic autobiographical recall (Levine et al., 2002; Piolino et al., 2002). Naturally, ABM is impaired in AD (e.g. Piolino et al. (2003); Starkstein, Boller, and Garau (2005)). Personal autobiographical memory in PD has not been as widely researched (Sagar, Cohen, Sullivan, Corkin, & Growdon, 1988; Smith, 1982), although deficits in episodic memory for public events and in source memory tasks have been reported (Gabrieli, Singh, Stebbins, and Goetz (1996); Johnson, Pollard, Vernon, Tomes, and Jog (2005); as cited by Souchay and Smith (2013)). To the author's knowledge, to date, only four studies have examined memory for personal episodic events and personal facts (Table 1-2). Two studies employed free recall and cue-word techniques. Cue-word methods involve providing the first event that comes to mind in response to a word cue, and then dating that event. The distribution of events across the lifespan is then compared (Piolino et al., 2002). In the

earliest study (Sagar et al., 1988), 23 PD patients (3 with PD-D and 20 non-demented) were given four minutes to provide detailed events from any lifetime period in response to ten high-frequency generic cues (e.g. tree, boy, bird, car). Participants were then spontaneously retested for recall 24 hours later. HC produced detailed specific events on the first day which were robustly reproduced the second day both with and without the aide of cues. The PD group produced comparatively fewer events on the first day, and showed a deficit in recalling these same memories on day two without cues. The detail of the previous day was restored when participants were prompted with generic and event specific cues (e.g. 'onyx'). Analyses across episodic epochs yielded unclear findings, with some PD patients recalling more memories from the most recent life period and others having a higher frequency of recall from remote periods. However, the impaired performance of the PD group was clearly characterized by deficits in recalling time-specific events, with events tending to be temporally generalized across related episodes. These findings suggested over-generality to be a key feature of ABM in PD.

Smith, Souchay, and Conway (2010) gained a similar impression in a study administering a modified version of the 'autobiographical fluency task' (Dritschel, Williams, Baddeley, & Nimmo-Smith, 1992) given to 16 PD and 16 healthy older controls. This task examines memory for both personal events and semantic recall of personal facts. Participants were given two minutes to recall as many names of non-related people (constituting semantic facts) as they could over five life periods, without repeating any names. They were also given two minutes to recall and briefly describe as many personal events as possible. Events were classified as specific if they occurred within 24 hours and contained some aspects of event-specific knowledge-type detail, or as generalized if they lasted longer than 24 hours or were events that fused into a narrative. PD patients recalled as many names as the older adult controls but produced fewer personal events overall. A gentle temporal gradient was

Table 1-2. *Studies researching personal autobiographical memory in Parkinson's disease. The order is chronological.*

Author(s)	Sample	Years Since Diagnosis, Motor Characteristics	Patients' Mean Age in Years (SD)	Cognitive Status	AM Measures	Main Results
Sagar et al., 1988	23 PD (20 PD-N, 3 PD-D) 37 HC	Duration - 7.9 Range - 1-19	PD: 64.0 HC: 62.2	BDS - 3.46	Modified Crovitz Personal Remote Memory Test	PD personal events recall impaired c/f HCs, particularly personal events from last 5 years.
Smith, Souchay & Conway, 2010	16 PD 16 HC	Duration - 6.0 Mild rigid-akinetic type H&Y - 1.9 (0.96) UPDRS III - 27.13 (13.67)	PD: 72.13 (5.85) HC: 72.5 (6.71)	Non-demented MMSE - 28.87 (1.02) Edu.*(y)*- 12.19 (2.64) HC: MMSE - 28.66 (1.44) Edu.*(y)* - 13.91 (4.21)	Autobiographical Fluency Task. 2 min recall of personal events over 5 life periods (0-18, 19-30, 30-last 5 yrs, last 5 yrs - excl. last 12 mths, last 12 mths). Measuring frequency of specific events (<24h) & general events (>24h / extended narrative) Personal facts – measuring frequency of names of non-related people associated with each time period	Personal events: PD fewer total events c/f HC ($p \leq 01$). PD fewer specific events c/f HC across all time periods ($p < .001$). HC & PD recall fewer specific events in recent time periods c/f more remote periods. Gentle temporal gradient more pronounced in PD - fewer specific events recalled c/f HC for recent time periods($p < .001$). Personal facts (names): no group differences. Both PD & HC recall fewer names in last two time periods ($p < .001$).
Souchay & Smith, 2013	16 PD 16 HC	Duration - 8.0 *(*16.28) Mild-moderate rigid-akinetic type H&Y - 2.9 UPDRS III - 26.18	PD: 75.18 (9.57) HC: 74.51 (7.86)	Non-demented MMSE ≥ 26 Edu.*(y)* - 10.87 *(*1.71) HC: Edu.*(y)*-12.63 (3.01)	Autobiographical Fluency Task. 3 min recall of personal events over 5 life periods (0-18, 19-30, 30-last 5 yrs, last 5 yrs - excl. last 12 mths, last 12 mths). Pt creates specific cues by giving memory a short title. Measuring frequency of specific events (<24h) & general events (>24h / extended narrative) across 3 consecutive phases: free recall, response to general cues, response to specific cues	PD group impaired in free recall phase and in general lifetime period cues. PD group same as controls retrieving memories to self-generated cues.
Nicolson, 2016	20 PD 15 HC	8.55 (5.24) H&Y - 2.55 (0.58) UPDRS III - 34.75 (14.38)	PD: 73.25 (6.53) HC: 74.27 (6.23)	ADAS-Cog - 6.54 (2.07) DRS-2 - 11.55 (3.15)	Autobiographical Memory Interview Assessing semantic memory and episodic memory over three life periods (0-18, 18-30, within last 5 years)	PD group unimpaired semantic memory c/f HC PD lower episodic memory scores across all time periods c/f HC ($p < .05$) PD group more impaired during childhood period c/f HC ($p < .01$, post-hoc) PD group more impaired during childhood than later periods. HC more impaired in later periods.

Abbreviations: ADAS-Cog = Alzheimer's Dementia Assessment Scale-Cognitive AM = Autobiographical memory; BDS = Blessed Dementia Scale; DRS = Dementia Rating Scale; HC = Healthy Controls; H&Y = Hoehn & Yahr Scale; MMSE = Mini Mental Status Exam; PD = Parkinson's disease; UPDRS III = Unified Parkinson's Disease Rating Scale.

observed in that both groups produced fewer specific events in more recent life periods, which was significantly more pronounced in the PD group compared to controls for the last two life periods (within the last five years, and within the last 12 months). Similar patterns have been observed in tests of recall for public events, where PD patients tend to show greater impairment in recalling and dating events during more recent decades (Sagar et al., 1988). Furthermore, when free recall for public events is compared with cued and recognition conditions (Venneri et al., 1997), the graduated levels of performance observed associate with degree of task difficulty, suggesting that recall deficits may stem from a failure in retrieval (Smith et al., 2010).

Building on these observations, Souchay and Smith (2013) sought to examine whether degree of cue ambiguity could influence retrieval in personal ABM, as it appeared to do in recall for public events. In an adaptation of their previous study, 16 cognitively unimpaired older adults with PD and 16 older controls were given three minutes to recall memories associated with five different time periods, and generated short titles for each memory. Participants were later asked to retrieve the same memories across three sequential conditions: free recall, in response to generic time cues, and in response to the self-generated cues. The performance of the PD group was impaired relative to the control group when retrieving the same memories in the free recall and general cue phases, but showed equivalency in performance when self-generated cues were used. This finding suggested retrieval of personal events may be the origin of impairment. Personally relevant cues may initiate a direct route to retrieving a memory that is not available to more generic cues, that instead requires a more cognitively demanding iterative search process (Souchay & Smith, 2013). More broadly, the evidence from cue-task assessments suggest an ABM deficit to be present in cognitively-normal PD, which is characterized by over-generality and difficulty recalling specific memories compared with healthy aged controls. There are however

methodological limitations to cue-based techniques including the artificial demands of the task, as people are required to produce a personal memory from a cue that may not hold much relevance to experiences in their lives (Piolino et al., 2002). Assessment of recall for personal facts is also constrained by frequency measures that use single-category examples (e.g. names of non-related people) as measures of overall semantic memory performance rather than a broader range of knowledge categories. On account of these limitations, contemporary ABM research in older adults has shifted from frequency-based, cue-word assessments to examination of episodic detail and quality of content, and measures of semantic memory that contain more than one type of fact (Piolino et al., 2006).

Initial work as part of the current study employed the Autobiographical Memory Interview (AMI) to examine episodic and semantic recall in 20 pre-MCI Parkinson's patients and 15 healthy age and education-matched controls (Kopelman, Wilson, & Baddeley, 1989; Nicolson, 2016). The AMI is one of the most widely-used measures of ABM in the existing literature, and was developed to negate the limitations of cue-word methods and accommodate assessment in neuropsychological settings, where episodic memory retrieval has long been regarded as a reliable neuropsychological marker of AD (Irish, Lawlor, O'Mara, & Coen, 2010; Piolino et al., 2002). The AMI's testing format is divided into a semantic schedule and an episodic schedule which covers three age periods (childhood, early adult and recent life). Memory for personal facts is measured using questions based on general knowledge (names of teachers, doctors, dates and places). The episodic schedule assesses the quality of nine autobiographical incidents divided across the three time periods. Participants are required to provide an event in response to a specific theme (e.g. incident at primary school, incident at one's own wedding, an incident involving doctors or care staff). Specific cues are given if participants cannot think of an event (e.g. a day out with a teacher; meeting your spouse). Scoring uses a content based approach, with a maximum of three

points awarded per event according to three main criteria, namely “what”, “where” and “when”. If all three elements are present, the event is considered to reflect retrieval from episodic memory (Irish et al., 2008).

Findings by Nicolson (2016) using the AMI showed semantic memory performance to be similar between the PD and control groups with both scoring highly across all time periods. The PD group performed more poorly in episodic memory recall across all three time periods compared with HC, showing a consistent deficit in detail recalled. Post-hoc analyses showed the PD group produced significantly relatively fewer childhood events compared with the most recent five years of life, which supported some earlier findings (Smith et al., 2010); but not all, such as those where PD performance yielded no clear trend at all (Sagar et al., 1988). Overall, these preliminary findings using the AMI indicate personal episodic memory deficits to be present in some cognitively normal PD patients when compared with a well-matched control group.

Although it is one of the most well-established interviews used in the AM literature, some limitations persist with certain aspects of the AMI’s testing format. Age related changes in PD memory content are not yet well characterized, and the exclusion of the decades between middle life and recent life status in the AMI may restrict the extent of its sensitivity to performance gradients across the life span. Additionally, the episodic ABM schedule uses a three-point ordinal rating scale to score events described in their spatio-temporal context. Awarding the maximum three points for an event is considered to reflect an episodic AM. However, it is possible to rebuild personal events from semantic memory without actually re-experiencing sensory-perceptual details that make a memory episodic (Piolino et al., 2006). Therefore the AMI episodic schedule is vulnerable to semantic contamination because its rating scale is unable to clearly discriminate between specific and more general levels of recall. The risk of ceiling effects across semantic and episodic schedules also cannot be ruled

out in cognitively normal populations (Piolino et al., 2002). This was a concern noted by Nicolson (2016, personal communication), the researcher who previously administrated the AMI at baseline in many of the cognitively unimpaired PD cohort tested in the current study. However, although mean scores were high, the AMI was still sensitive enough to discern impaired episodic memory recall in the PD cohort compared with HC.

Other tests, such as the Autobiographical Interview by Levine et al. (2002), collapse the semantic and episodic memory distinction as far as schedule format is concerned. Participants are invited to produce specific personal memories that occur across each of five different life periods across the life span, which are then audio recorded and transcribed for detailed analysis of content. Scoring involves analyzing events across several subcategories of detail that are proposed to reflect episodic re-experiencing of an event; including environmental, spatial, temporal, perceptual, sensory, emotional and metacognitive details. These details are separated from information containing semantic facts or repeated information extraneous to the main event. In comparison, the Episodic Autobiographical Memory Interview (EAMI; Irish et al., 2008) retains the AMI's semantic and episodic dual-schedule approach but also invites personal memories that contain specific details relating to event, time and place which are later transcribed for component analysis and scoring. Emphasis is placed on examining the presence of contextual details across several discrete phenomenological categories of detail which are considered integral to the experience of episodic recall (Irish et al., 2008; Irish et al., 2010; Levine et al., 2002). The appeal of the EAMI is the checklist approach, which allows a high level of contextual detail to be probed methodically and with consistency (Irish et al., 2010; Moscovitch, Yaschyshyn, Ziegler, & Nadel, 2000). Hence the EAMI was used at end of trial testing in the current study.

Within the AMI a number of episodic enquiries are structured around specific topics. For example, an episodic item from the Early Adult Life time period asks participants to

recall the first time they met someone new. The most recent life period focuses on present and past engagement with hospitals and care institutions. The AMI was validated using amnesic patients of various clinical diagnoses (Conway & Pleydell-Pearce, 2000; Kopelman et al., 1989; Piolino et al., 2002), and in this population such themes would be appropriately specific. However, as with the cue word method (Piolino et al., 2002), they may not carry over to the experiences of more active, relatively unimpaired populations. Incorporation of generic themes may accommodate a broader spectrum of experiences than the AMI facilitates, and thereby increase the likelihood that participants produce memories exemplifying their recall ability within a given life period. The EAMI negates the use of specific themes for episodic event recall, but offers cues if an event is not spontaneously forthcoming (Irish et al., 2008). In doing this, the EAMI incorporates adaptations of themes used in an autobiographical memory interview by Piolino et al. (2002); Piolino et al. (2006). Generic themes of events, for example, related to a trip or journey, or a family event, are rotated across several time periods that cross the life course.

Despite these limitations, a significant advantage of the AMI is its brevity in administration time, which carries utility within the neuropsychological testing environment. It took no longer than forty minutes to complete and in the initial work by Nicolson (2016) was administered comfortably within the same session as a multi-domain cognitive screening battery. Potential improvements to the AMI when administering to an unimpaired population relate to the examination and scoring of episodic events, where greater analysis of contextual detail would help to identify truly episodic recall from semantic artefact. Broadening event themes would increase its applicability to the experiences of a wider population; and the incorporation of an additional life period in adult life would allow for a more nuanced examination of autobiographical episodic and semantic recall gradients within a relatively understudied PD cohort. However, these elements can be drawn from other well-established

autobiographical memory schedules, and have been incorporated into the post-trial autobiographical memory testing schedule for the current study.

1.6 The current study

The current study examined performance on tasks measuring autobiographical memory and ToM in a cohort of well-characterized non-MCI PD patients. They were recruited into a two-armed randomized controlled trial designed to assess the effects of a lifestyle intervention package on cognitive performance. Performance of the PD groups was compared with a group of healthy age, sex and education-matched older adult control participants at baseline and under blinded testing conditions at end-of-trial. The same sample of PD and HC participants used in the initial study by Nicolson (2016) was included in this study, with an additional 21 PD participants and 13 HC recruited and entered into the PD Enrichment trial over the ensuing ten months.

Cognition was assessed using a range of neuropsychological batteries administered at baseline and end-of-trial. The false belief cognitive card sequencing task (Langdon et al., 1997) was used to assess cognitive ToM at baseline and follow-up. The AMI (Kopelman et al., 1989) was used as a standard instrument to assess autobiographical episodic and semantic memory performance at baseline. End-of-trial autobiographical memory testing incorporated the AMI into the EAMI (Irish, Lawlor, O'Mara, & Coen, 2011b), which was introduced because of its methodically straightforward yet conceptually robust episodic scoring schedule and structural compatibility with the AMI. The thematic scaffolding required for AMI longitudinal performance comparisons was incorporated from testing protocols developed by Piolino et al. (2002); Piolino et al. (2006). The original EAMI excludes themes in favour of unrestricted recall conditions although its prompts are also drawn from Piolino et al. (2002); Piolino et al. (2006).

Part of this trial's intervention package included a series of personal episodic memory elaboration sessions. The scientific rationale for this was based on a theory of spreading activation of semantic and episodic memory networks (Foster et al., 2017), in which repeated activation of an episodic memory may strengthen connections to other associated events, thoughts and feelings, which can then be elaborated so as to further strengthen and perpetuate the spread of activation to additional associated nodes and networks. In this way, it was anticipated that the activation of frequently and less-frequently recollected episodes would be increased and strengthened across time. The methodology behind the sessions used exploration of episodic details that drew upon descriptive, emotional and metacognitive aspects of recall (Irish et al., 2008). A qualitative 'quilting' narrative technique assisted with accessing less vividly recalled memories (Moore & Davis, 2002). As a supplementary activity, participants engaged in hand-drawn mapping exercises of familiar childhood environments in order to stimulate DMN regions associated with navigational and spatial orientation (Buckner & Carroll, 2007).

1.7 Study aims

To reiterate, the current study explored the effect of an eight-month cognitive and physical activity lifestyle intervention on performance in measures of cognitive ToM and autobiographical memory in a group of non-MCI participants with Parkinson's disease randomized to either an "active enrichment" treatment arm or "passive enrichment" control arm. The primary aims of the study were as follows.

1. To examine whether PD participants in an "active enrichment" intervention arm show relative improvement in these measures by comparison with PD participants in a "passive enrichment" arm.
2. To compare performance on these measures with a group of healthy older-adult control participants, at baseline and at end-of-trial.

Part of the novelty of this research was to examine an adapted version of the EAMI (Irish et al., 2008) for the first time in non-MCI PD patients, who could be further characterized as having variable risk for future progression of cognitive decline, based on an initial "screening risk score" (Myall et al., 2015). This was also the first time that the Theory of Mind card sorting task developed by Langdon et al. (1997) had been used to assess cognitive status of PD patients at baseline and at end-of-trial in a randomized controlled trial.

Chapter 2: Method

2.1 Participants

Participants were recruited from a larger population of 238 PD patients involved in a longitudinal Health Research Council (HRC) study of progression to PD-MCI, run by the New Zealand Brain Research Institute. The process of recruitment, exclusion and retention is shown in Figure 2.1. A total of 196 patients received a Level I cognitive screening assessment to establish their suitability for the HRC longitudinal study. Of these, 125 underwent additional Level II neuropsychological testing to confirm non-MCI cognitive status. PD participants who satisfied the following inclusion criteria were invited into the Enrichment study: a diagnosis of idiopathic PD as defined by the U.K. Parkinson's disease society brain bank clinical diagnostic criteria (Hughes, Ben-Shlomo, Daniel, & Lees, 1992); aged 60 - 85 years of age; and fluency in written and spoken English. The exclusion criteria included (a) the presence of mild cognitive impairment (PD-MCI) or dementia (PD-D; Wood et al., 2016); (b) presence of co-morbid atypical movement disorders; (c) concurrent participation in studies involving pharmacological interventions; (d) current use of cognition-affecting medication; (e) a history of learning disabilities, substance misuse, or major medical, psychiatric or neurological illness within the past twelve months. A total of 44 eligible patient volunteers then completed Enrichment study baseline cognitive assessments. They were assessed in the mornings during 'ON' state, with symptoms mostly managed with anticholinergic, levodopa or other dopamine agonists. These 44 PD participants represented the final sample and were randomized into the trial. Their trial entry age is presented in Figure 2.2, below. A comparison group of cognitively and physically healthy sex, age (±5y) & education-matched (±4y) non-PD control participants (HC; *n*=28) was also recruited from the institute's volunteer database.

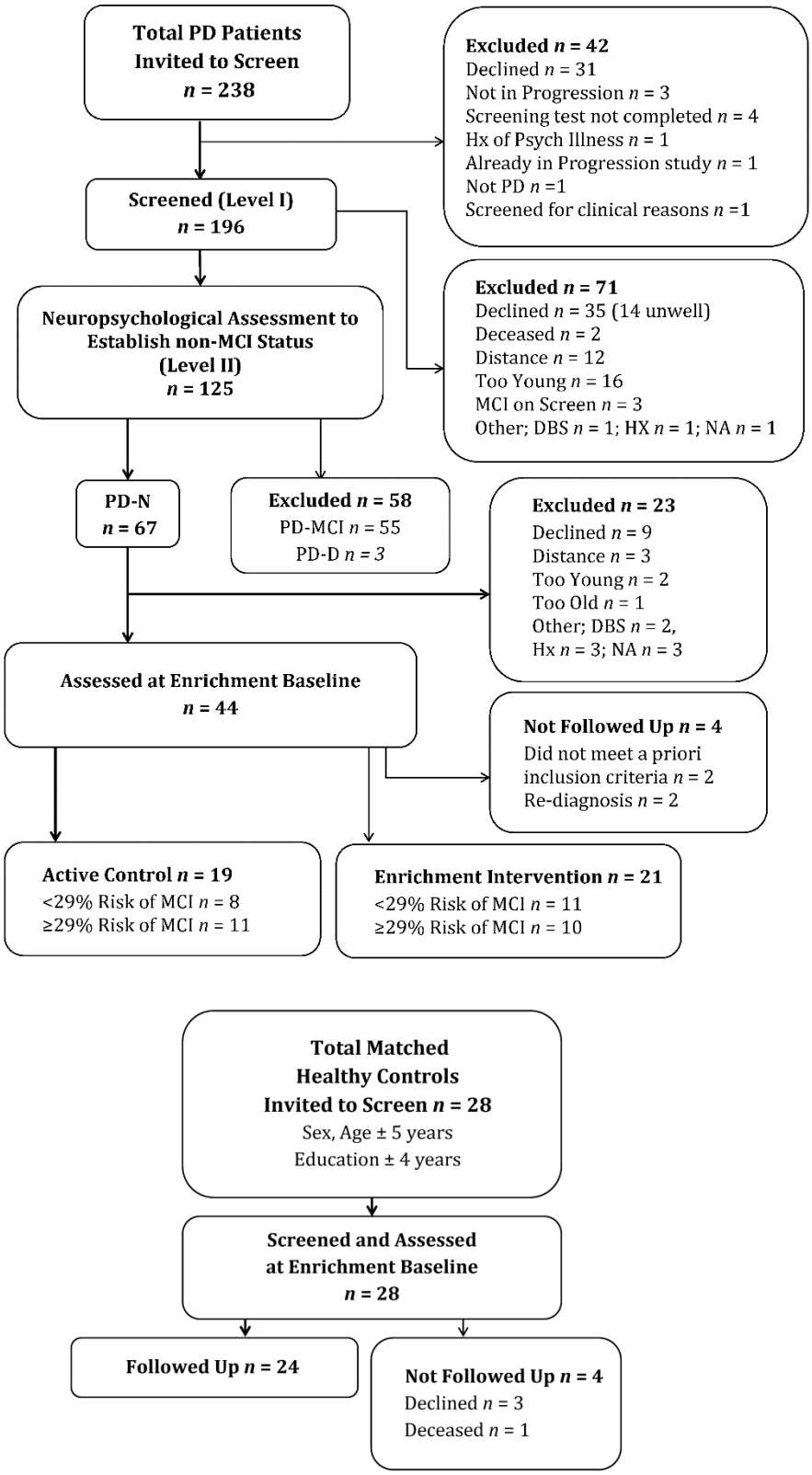


Figure 2.1: Process of recruitment and selection of PD and HC participants.

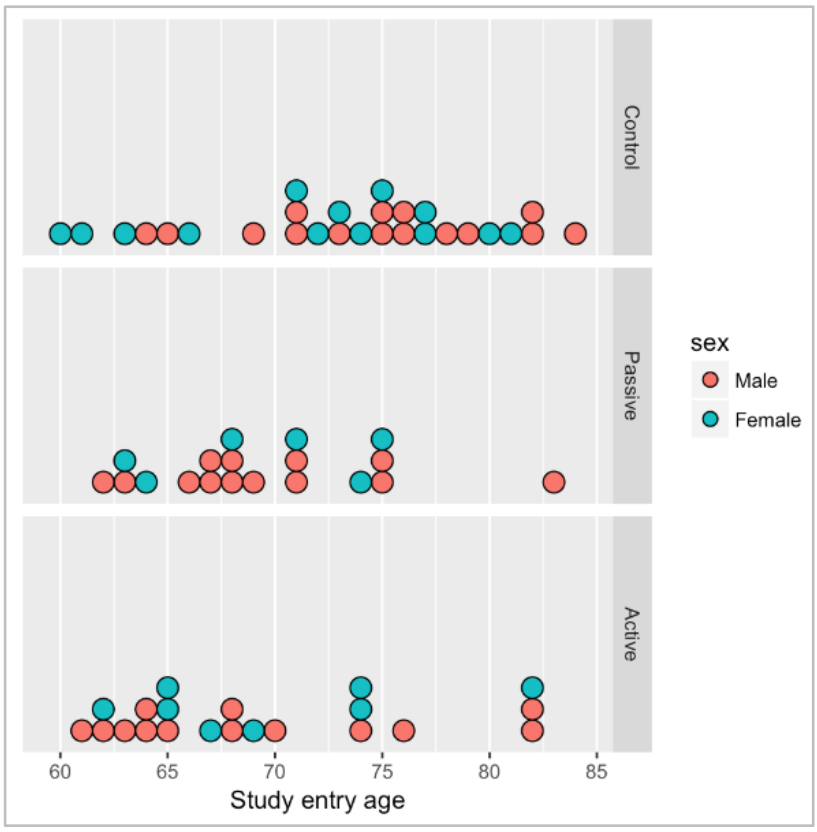


Figure 2.2: Study entry age for male and female PD-active, PD-passive and HC participants.

2.2 Ethics

Informed consent was given by all participants, and a $20 MTA voucher was provided as reimbursement for travel costs for every neuropsychological testing session at the institute. The Enrichment study was approved by the New Zealand Health and Disability Ethics Committee (HDEC reference number 15/NTB/161). The screening process concerning Progression to PD-MCI and PDD was approved by the HDEC (reference number URB/09/08/037).

2.3 Randomization procedure

Randomized allocation of PD participants into the 'PD-active' intervention arm (comprising combined cognitive and physical exercises) or 'PD Passive' control arm (usual care plus monthly researcher contact) was done in four blocks of 8-12 participants following completion of baseline assessments (Table 2-1). This process was undertaken using computer

generated concealed allocation and stratification of age (60-72y vs 73-85y), duration of PD (<8y vs >8y), and high vs low risk of conversion to PD-MCI within a four-year period. Risk scores were calculated using an a priori model of risk generated from a large separate NZBRI longitudinal study cohort and the neuropsychological screening battery described in the next section (Myall et al., 2015). A risk score of 29% was determined as the optimal ROC sensitivity and specificity cut-off point for discriminating between patients who would and would not convert to PD-MCI across the next four years. To accommodate the sequential recruitment of participants into the study, three sets of paired high vs. low risk scores were used (29-49% vs >49%; 22-28% vs 15-21%; 0-7% vs 8-14%). Groups were well matched on age and education with no significant differences between PD groups.

Table 2-1. *Breakdown of key enrichment trial time points for each randomized PD group.*

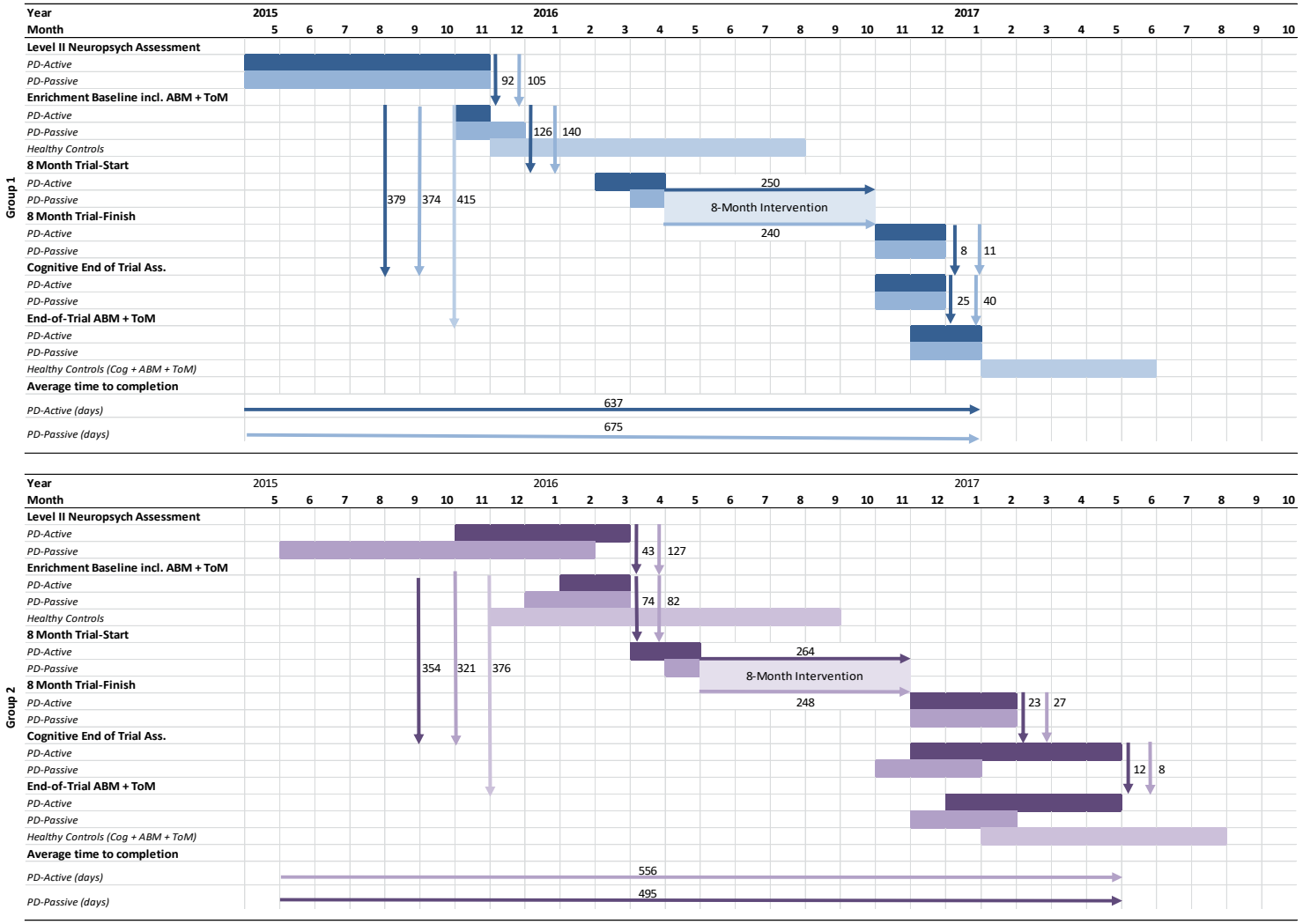
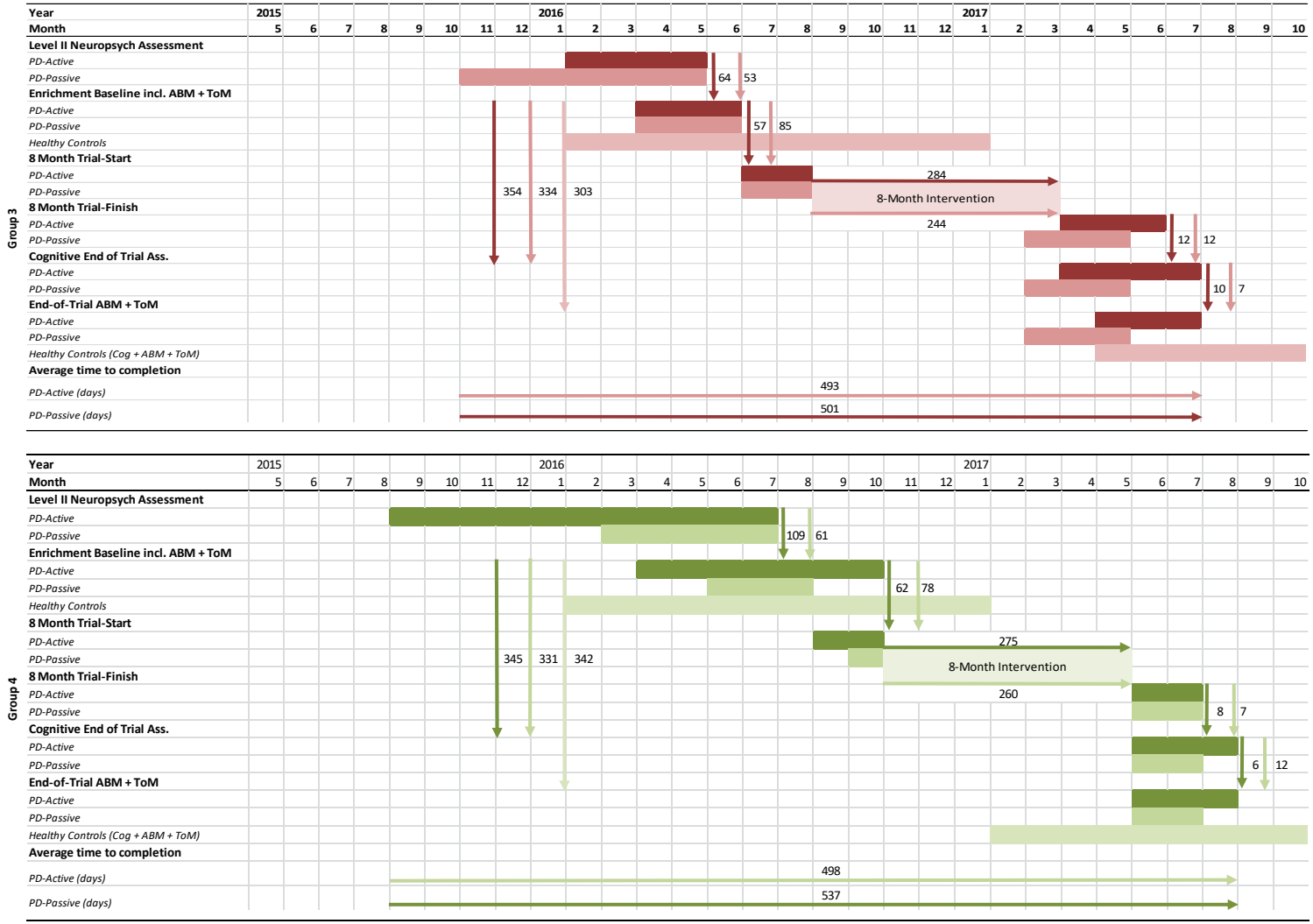


Table 2-1 contd.



2.4 Materials

2.4.1 Initial cognitive screening assessment

2.4.1.1 Initial cognitive screening test

The initial cognitive screening assessment formed part of the wider HRC PD Progression study. Sessions lasted 30 minutes, and consisted of the Montreal Cognitive Assessment (MoCA, Nasreddine et al., 2005) as a measure of global functioning; the Delis-Kaplan Stroop word naming, colour naming, and colour-word interference subtest (Delis, Kaplan, Kramer, & Ober, 2001); written Trail Making Test (TMT) Version A and Version B, and the Test of Everyday Attention (TEA) map search task (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1994). When adjusted for age, this screening battery has been shown to provide a sensitive composite measure of probability of future progression to PD-MCI and was used in the generation of risk scores (Myall et al., 2015). All screening assessments were undertaken by a project researcher at the NZBRI.

2.4.1.2 Neuropsychological assessments to establish non-MCI status

To establish non-MCI cognitive status, PD participants were then given a comprehensive neuropsychological testing battery in two separate sessions at the NZBRI. Administration of tests adhered to procedures specified in the appropriate testing manuals. The testing battery was consistent with the Movement Disorders Society (MDS) Task Force Level II diagnostic criteria for PD-MCI by including at least two tests across five cognitive domains (executive function, attention and working memory, visuospatial function, memory and learning, language; Litvan et al. (2011); Wood et al. (2016)).

Executive function was assessed using TMT Part B; D-KEFS letter, category and alternating category fluency tasks; Stroop colour-word interference subtest (Delis et al., 2001); and the action verbal fluency test (Piatt, Fields, Paolo, & Tröster, 2004). Attention and

working memory functions were determined using Digit span forward and reverse ordering (Wechsler, 2008); the TEA map search task (Robertson et al., 1994); TMT Part A; and Stroop word and colour naming subtests (Delis et al., 2001). Visuospatial functioning was evaluated using Benton's Judgement of Line Orientation (Benton, Sivan, Hamsher, & Spreen, 1994); Visual Object and Space Perception fragmented letters subtest (Warrington, James, & Thames Valley Test, 1991); Rey-Osterrieth Complex Figure copy trial (Meyers & Meyers, 1995); Mini Mental State Examination intersecting pentagon copying test; and the picture completion subtest of the Wechsler Adult Intelligence Scale - Fourth Edition (Wechsler, 2008). The domain of memory and learning was assessed using California Verbal Learning Test - Second Edition (Delis et al., 2001) and Rey-Osterrieth Complex Figure immediate and delayed recall trials (Meyers & Meyers, 1995). The fifth domain, Language, was examined with the language component of the ADAS-Cog (Mohs et al., 1997); the Dementia Rating Scale-2 similarities sub-test (Jurica, Leitten, & Mattis, 2001); and the short-form of the Boston Confrontation Naming Test (Kaplan, Goodglass, Weintraub, & Brand, 1983).

2.4.2 Enrichment study baseline neuropsychological assessments

HC and PD participants who satisfied Enrichment study inclusion criteria were invited to complete a baseline cognitive assessment which took approximately two hours. For PD participants, assessment included the 15-item Geriatric Depression Scale (GDS-15; Yesavage et al., 1982) and Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the 14-item Starkstein Apathy Scale as a measure of psychiatric status. PD participants also received the Brief Visuospatial Memory Test - Revised (BVMT; Benedict, 1997) and the written version of the Symbol Digit Modalities Test (Smith, 1982). Semantic language was evaluated with the Sydney Language Battery confrontation naming, word comprehension, semantic association and single word repetition subtests (Savage et al., 2013). Non-motor symptoms were assessed using the REM Sleep Behaviour Disorder Screening Questionnaire,

Parkinson's Disease Sleep Scale – Second Edition and the PD Non-Motor Symptoms Questionnaire. An in-house Lifetime Activities Questionnaire collected information from all participants on type and degree of exposure to physical and non-physical activities across the lifetime. HC participants completed a baseline cognitive screening assessment over a single two and a half-hour session at the institute, which included the MoCA, Stroop, Trails A & B, TEA Map Search, SDMT, and HADS. PD and HC participants were also tested for theory of mind and autobiographical memory performance, described in the following sections.

2.4.2.1 Autobiographical memory interview

The Autobiographical Memory Interview (AMI; Kopelman et al., 1989) was used as a measure of baseline episodic and semantic ABM performance. This semi-structured questionnaire is divided into semantic and episodic schedules which measure recall of personal facts and specific event incidents across three life periods: Childhood, from infancy to adolescence (ages 0-18); Young Adulthood (ages 18-early thirties); and Recent Life status (within the past 5 years). The organization of the AMI semantic memory schedule into life periods and its subsections is presented in Table 2-2. For each subsection, semantic enquiry was followed by one episodic memory event enquiry (excepting Last Christmas; nine events in total).

***Table 2-2**. Organization of the AMI semantic schedule across life periods.*

Life Period	Period Score Total	Subsection Themes	Sub-Section Total	Items
Childhood	21 pts	Before school	5 pts	Address, names of three friends
		First/Primary school	8 pts	Name and location of school, age at starting, address, names of three teachers or friends
		Main secondary school	8 pts	Name and location of school, number and level of exams passed, address, names of three teachers or friends
Early Adult Life	21 pts	Career	8 pts	Name of firm or college, qualifications obtained or first job, address, names of three friends or colleagues
		Wedding: own or another's	9 pts	Whose, where, when, address before and after wedding, names of best man, bridesmaid, bride's maiden name
		Children	4 pts	Names of two children, dates and locations of birth
Recent Life	21 pts	Present hospital	8 pts	Name and location of present hospital, date of last attendance, names of three staff or patients, current address
		Previous hospital	8 pts	Name and date of previous hospital admission, address at that time
		Last Christmas	2 pts	Where last Christmas was spent and who with, names of three visitors or relatives seen in last year
		Holidays or other journeys in last year (or within last five years)	3 pts	Destination, date, name of one travel companion

The AMI episodic memory schedule requires participants to provide memories for nine incidents ('events') that occurred across the three life periods, each related to particular themes (Table 2-4, pp.49). At the commencement of the episodic schedule, participants were read the following script, adapted from Piolino et al. (2002):

''For each event, describe it out loud and with as much detail as possible, what happened, as if you are able to relive it: what you did and what you felt, the circumstances, when, with whom, where and how it happened. For example, if you are recalling holidays at

the seaside, you must avoid general descriptions. Rather, give precise memories of a particular event which happened on a day during these holidays.'

Participants were reminded regularly thereafter that their recollections should be described with as much detail as possible. For each episodic event enquiry, participants were firstly given a period of time to engage in free recall. If an incident was not forthcoming, they were prompted with cues provided in the AMI schedule (Kopelman et al., 1989, p. 55; Table 6). Episodic incidents were scored on a 0-3 scale with one point awarded for the provision of each of three elements: an isolated, one off-event lasting less than a day; where it took place geographically; and when it occurred (specific age or year or time of day). All interviews were recorded using the AMI scoring booklet with audio recorded on a Zoom H4N recorder.

2.4.2.2 Theory of mind card sorting task

Theory of mind performance was assessed with a cognitive theory of mind card sorting task (Langdon et al., 1997). This task presents a series of mixed-up stories on black and white cartoon illustration cards (21cm x 15cm) which participants must re-arrange to form logical sequences of events. There are four conditions divided evenly across 16 stories, with the scenes of each story depicted across four cards. A False Belief condition is compared with three control conditions that screen for sequencing errors caused by factors other than potential ToM deficits. The False Belief stories require the participant to understand the behaviour of a character whose actions in the story depend on their naivety to a salient event that has just taken place. The Mechanical condition requires the ordering of objects interacting causally. For the Social Script condition, characters are involved in a daily activity; and in the Complex Reasoning condition, characters are depicted in routine activities where there is an obvious misleading clue plus another more subtle clue which the participant must identify in order to correctly sequence the story.

As presented in Appendix A, each participant received the same scripted instructions Participants were then sequentially presented with each story. Cards were placed face down in a row of four in a fixed semi-randomised order, as shown on the scoring sheet presented in Appendix B. Participants were asked to turn the cards over, rearrange them and signal when they were finished. The time taken for each story to be reordered to the participant's satisfaction was recorded using a stop clock. The sequencing of cards for preparation and scoring was aided by coloured dots and numbers that were printed discreetly on their reverse side and which were interpretable only to the assessor. Each condition was scored from a maximum of 24 points.

2.4.3 Enrichment trial activities

Following baseline testing, participants entered the Enrichment trial in four groups staggered over the course of twelve months (Table 2-1) between March and October 2016. Over an eight-month period, PD-active participants received weekly physical exercise sessions and cognitive exercises in fortnightly manuals. PD-passive participants received scientific news articles and related questions on a monthly basis. For the duration of the trial, all PD participants completed weekly thinking, memory and physical activity diaries, monthly questionnaires and a dietary nutrition questionnaire. For HC participants, no contact was made in the interceding months between baseline and end-of-trial testing.

2.4.3.1 Physical exercise training

On a weekly basis in groups of three or four, PD-active participants attended a Christchurch Physiotherapy Centre gym for one-hour exercise classes supervised by Otago university physiotherapists (Mulligan et al., 2018). The classes encouraged social engagement and involved warm-ups with strength, balance, resisted and aerobic circuit exercises. Participants were encouraged to exercise to a level of exertion that would improve fitness over time whilst

maintaining heart rate within safe parameters. This was represented visually as a gym wall poster of exertion emoticons (Figure 2.3).

2.4.3.2 Cognitive exercise folders

As part of the intervention, PD-active arm participants were given cognitive exercise folder manuals on a fortnightly basis over the eight-month trial period, which contained approximately one and a half hours of exercises per manual (three hours per fortnight). Manuals included different novel exercise tasks designed by the research team, which were to be completed with the supervision of a support person. Tasks were designed to become increasingly more challenging with successful progression so that sense of achievement was maintained. To ensure they were not too difficult, they were rated on their level of challenge by participants (i.e., 'too easy'; 'easy'; 'ok'; 'hard'; 'too hard'), and were adjusted on a case-by-case as required. Overall, twenty different tasks were integrated into eighteen manuals to form a comprehensive, multi-domain cognitive exercise intervention package. Sixteen tasks stimulated externally-directed modes of thought and engaged the attention, executive function, memory, visuospatial and language networks. Four exercises activated internal modes of thought and stimulated the DMN. These included Reading the Mind in the Eyes and Faux Pas story tasks, as well as moral dilemma reasoning and envisioning future events (Appendix C). The salience switch network was stimulated by switching between exercises that engaged internal and external modes of cognition respectively. Disseminated task accessories included cards, counting timers, coloured shapes and letter-grid shakers.

Figure 2.3: Exertion emoticons for participants at exercise session (target: 13).

2.4.3.3 Episodic memory elaboration sessions

As part of the cognitive exercise programme, PD-active participants were invited to take part in a series of six memory elaboration sessions which were conducted by the author at participants' homes or in a quiet room at the institute. These sessions took place every three to four weeks over the second four months of the Enrichment trial. Their aim was to encourage activation of key DMN regions by rehearsing and elaborating three episodic events given by participants at the baseline autobiographical memory assessment, derived from each of the three life periods examined in the AMI:

i. An incident from high school.

ii. An incident at a wedding during the participant's twenties.

iii. A recent trip or journey from within the last six years.

If a memory had not been provided at baseline testing, an alternative event was identified in the earliest session to enable the elaboration exercises. Critically, three new incidents were also identified during the earliest elaboration sessions, which were needed to replace the elaborated baseline events, for later end-of-trial testing. These incidents were selected based on their similarity to the original baseline events in their level of detail. They were discretely noted down but not rehearsed with the participant at any stage.

Participants also selected a photo depicting a memorable personal event from the previous ten years, which was elaborated over two visits. To exercise spatial domains, an additional activity included sketching layouts of childhood homes, schools or neighbourhoods over two visits, with the second session used to add fresh layers of detail or elaborate associated episodic recollections (Appendix D). A variation of this exercise involved reviewing printed Google maps of areas participants lived or regularly frequented, to encourage reflections about environmental and socio-cultural landscapes plus activities of the time. Appendix E presents extracts of transcribed baseline events, Appendix F, transcribed excerpts of dialogue from elaboration sessions. Participants were also encouraged to think about various other aspects of their lives at the time of these events, including accommodation lodgings, pastimes, environments, activities and so forth. Two events were elaborated per visit with the three baseline events revisited four times in rotation across the six sessions (Table 2-3).

Table 2-3. *Schedule of elaboration sessions for PD-active participants.*

			Session					
			1	2	3	4	5	6
Event	(1)	High School	♦	♦	-	♦	♦	-
	(2)	Wedding	♦	-	♦	♦	-	♦
	(3)	Recent Journey	-	♦	♦	-	♦	♦
	(Photo within the last ten years)		-	-	♦	♦	-	-

Note. Sessions were scheduled every three-to-four weeks, four months into the trial for each PD-active participant.

The overarching aim of the memory elaboration sessions was to stimulate the DMN by encouraging the frequency of reminiscences during and between visits and elaboration of recalled details over time. Participants were encouraged to pay attention to the phenomenological aspects of episodic recall; especially visual imagery, emotional contexts, temporal, spatial and sensory details, as well as reflect upon the thoughts and emotions of other agents represented in their recollections. Participants were also encouraged to close their eyes in order to reduce distractions from external stimuli, and augment retrieval of visual imagery (Nori, Bensi, Gambetti, & Giusberti, 2014; Vredeveldt, Hitch, & Baddeley, 2011).

Sessions were loosely structured to accommodate spontaneous recollections and were conducted in a conversational manner using open-ended, non-leading questions to minimize suggestive questioning (Nori et al., 2014; Wright & Holliday, 2007). Based on a collaborative 'quilting' technique (Moore & Davis, 2002), any words or details that were repeated or followed by hesitancies or utterances were encouraged for further elaboration or noted down, so that the related subject material could be revisited in forthcoming sessions. These conversational inflections may have signalled the resurfacing or activation of personally salient events to be explored further. Any unpleasant memories were avoided. To prepare for each elaboration session, a list of open-ended questions was generated for each event which drew upon the progress and departure points of the previous session. This preparatory process

was aided by recording each session (with participant consent), and note taking. Equipment included an H4N microphone recorder, notebook, pens, pencils, paper.

In total, 18 of the 21 PD-active participants completed the full six sessions; one participant completed five sessions and one completed four. Across all participants, approximately 1360-1365 minutes (23 hours) was spent elaborating a high school event from Childhood; 1395-1400 minutes (23.3 hours) elaborating a wedding event from Young Adulthood; and 1361 – 1365 minutes (22.6 hours) elaborating a recent journey. Events depicted in photos were elaborated for between 465-470 minutes (7.8 hours). Audio for eight sessions was lost and is not included in these time summaries.

2.4.3.4 Weekly diaries and monthly questionnaires

In the interests of maintaining researcher contact, monitoring symptoms throughout the trial and ensuring a well-characterized PD cohort, a series of weekly and monthly self-administered questionnaires were completed by both groups throughout the trial. Weekly diary sheets were used to record the types of thinking, memory, social, and physical activities participants had engaged in each day, as well as the amount of time they had spent on each activity. Four additional questionnaires were completed on a monthly basis to monitor PD symptoms. These included the PDSS-2, PD-REM sleep behaviour questionnaire, PD-NMS scale, and the Parkinson's Well Being Map (UCB, 2013), which screens PD motor and non-motor symptoms across seven psycho-social domains of wellbeing. A nutritional questionnaire was completed every three months to capture details relating to participant weight, diet, dining habits and their consumption of vitamin and mineral supplements ('Screen', Keller, Haresign, & Brockest, 2007). Updates to medications were also checked on a monthly basis.

2.4.3.5 Scientific magazine articles

To encourage regular contact with the research team, Active-control participants received monthly paragraph-sized summaries of interesting science articles recently published in reputable magazines (e.g., New Scientist), which were accompanied by three questions relating to the content of the articles. These were completed by participants and emailed or posted back to the research team.

2.4.4 Enrichment study end-of-trial neuropsychological assessments

After completion of the active phase of the Enrichment study, PD participants returned to the institute for two 120-minute end-of-trial cognitive assessments, which involved repeating most of the pre-trial Level II and Enrichment baseline tests, including the Theory of Mind card sorting task and a revised ABM testing schedule. The revised ABM schedule comprised an amalgamation of the AMI with the semantic and episodic subscales of the EAMI which is described in the following section. All end-of trial PD testing was conducted under blinded conditions.

In the first assessment session, general cognitive functioning was reassessed with the Montreal Cognitive Assessment. Executive function was assessed using TMT Part B; Stroop colour-word interference subtest and the action verbal fluency test, Attention and working memory functions were investigated with the TEA map search task; TMT Version A; Stroop word and colour naming subtests the Symbol Digits Modality Test. Visuospatial memory and functioning was evaluated using Benton's Judgement of Line Orientation; Rey-Osterrieth Complex Figure copy trial; the BVMT and the Mini Mental State Examination (Tombaugh & McIntyre, 1992) intersecting pentagon copying test. The domain of memory and learning was assessed using California Verbal Learning Test - Second Edition, and Rey-Osterrieth Complex Figure immediate and delayed recall trials. The Language domain was examined with the language component of the ADAS-Cog; the verbal fluency task; the Dementia

Rating Scale-2 similarities sub-test; the visual association test; and the short-form of the Boston Confrontation Naming Test. Psychiatric wellbeing was re-assessed using the 15-item Geriatric Depression Scale (GDS-15), Starkstein Apathy Scale, the Hospital Anxiety and Depression Scale (HADS) and the Parkinson's Disease Questionnaire (Jenkinson, Peto, Fitzpatrick, Greenhall, & Hyman, 1995). In the second cognitive testing session, the Theory of Mind card sorting task and the revised ABM testing schedule (comprising the AMI and EAMI), was administered. HC participants completed a single end-of-trial assessment over a two and a half-hour session at the institute. They were administered the ToM card sorting task and revised ABM testing schedule, and the cognitive screening battery (the MoCA, Stroop, Trails Version A & Version B, and TEA Map Search) as well as the SDMT, BVMT and HADS. HC participants were assessed at baseline and end-of-trial assessment by Nicolson (2016) and the author. Baseline ToM and AMI testing for PD participants was conducted by Nicolson (2016) and the author.

2.4.4.1 Autobiographical memory retesting

Personal semantic and episodic memory retesting was undertaken using a combined interview protocol which represented an amalgamation of the Autobiographical Memory Interview (AMI; Kopelman et al., 1989); and personal semantic and episodic subscales of the Episodic Autobiographical Memory Interview (EAMI; Irish et al., 2008, Appendix G; H). This was possible because of design similarities in terms of overlap of life periods examined and the dual-schedule distinction between episodic and semantic declarative memory components. A small modification to the EAMI episodic subscale checklist involved the addition of four episodic event themes to guide participant memory selection. This was done to facilitate comparisons between baseline and end-of-trial performance, because the AMI restricts recall to specific topics whereas the EAMI does not use topic parameters at all, instead offering prompts when required. Therefore, four event topics compatible with both

the baseline enquiries of the AMI were drawn from Piolino et al. (2002) and added to the retesting schedule (Table 2-4). As a precautionary measure to preserve blinded testing conditions, the Recent Life period was adjusted to span the previous six years and exclude the twelve months preceding test date for five question items (S.4.4.1.- S.4.4.5). This placed activities related to the Enrichment trial outside the time range under investigation, thus reducing the risk of divulgence of arm allocation. Akin to the EAMI approach, a fourth, Later Adulthood period was also added which was not included in AMI baseline assessment. In total, four life periods were examined for semantic and episodic memory recall performance at end-of-trial assessment: Childhood (age 0-18), Early Adulthood (age 18-30), Later Adulthood (age 45 – 6 years ago), and Recent Life (between six years and 12 months ago). Three episodic events were assessed within each life period. The Childhood life period was separated into three age bands: Before School (age 0-five), Primary School (age five-11), High School (age 11-18) with one episodic memory event allocated to each age band. Because of considerations to time and interview length, a Middle Adulthood life period (age 30-45) was not included in end-of-trial assessment.

Table 2-4. *Baseline and end-of-trial episodic memory testing schedules with event item topics and prompts.*

	Baseline (AMI)	End-of-Trial (AMI + EAMI)
	Childhood (Age 0 - 18)	
Event 1.1.	Before starting school (age 0 - 5) First memory? Involving a brother or sister?	Before starting school (age 0 – 5) First memory? Involving your family, a brother or sister? A trip somewhere? A church event?
Event 1.2.	During primary school (age 5 - 11) Involving a teacher? Involving a friend?	During primary school (age 5-11) Involving a teacher? Involving a friend? A church event?
Event 1.3.	During high school (age 11 - 18) Involving a teacher? Involving a friend?	During high school (age 11-18) Involving a teacher? Involving a friend? Your confirmation?
	Early Adulthood (Age 18 - early thirties)	
Event 2.1.	From this (sic) wedding An incident involving a guest? An incident at the reception?	Related to a wedding or another type of family occasion A family holiday? The day of a birth?
Event 2.2.	A first encounter with someone while in your twenties Meeting someone in an interview? Meeting someone on holiday or at work?	Related to a specific person A first encounter with someone? A first meeting with a spouse? A day with a friend?
Event 2.3.	From college or the first job Your first day at work or college? An incident with a friend?	Related to college or professional life Your first day at work or college? An incident with a friend? A day with a teacher?
	Later Adulthood (Age 45 - six years ago)	
Event 3.1.		Related to a trip or journey At the place you visited? Involving someone you met? While you were travelling?
Event 3.2.		Related to a family event or occasion A birthday? Christmas day? A death?
Event 3.3.		Related to professional life or retirement Something unusual that happened at work? A day with your grandchildren? A day you went somewhere special?
	Recent Life (within last five years)	**Recent Life (within last six years, excl. last 12 months)**
Event 4.1.	Whilst at hospital or at institution Involving the other patients? To do with the doctors or nurses?	Related to a specific person An incident which occurred at hospital? Involving a neighbour? Involving a friend, a doctor or nurse?
Event 4.2.	Involving a relative or visitor in the last year A visit by or to a relative? Involving some news about a relative?	Related to a family event or occasion An incident involving a relative? Involving a visit somewhere? On a family holiday?
Event 4.3.	Related to a holiday or journey At the (sic) place you visited? Involving someone you met?	Related to a trip or journey At a place you visited? Involving someone you met? While you were travelling?

Abbreviations: AMI=Autobiographical Memory Interview; EAMI=Episodic Autobiographical Memory Interview.

The EAMI builds upon the AMI's three-point episodic memory scoring scale with the Episodic Subscale Checklist, which investigates the contents of any given memory using a score range of seven points. This score total reflects seven discrete categories of contextually specific detail, which are regarded as indicators of the episodic experience of 'reliving' of an event from memory (Irish et al., 2008; 2010; Table 2-5, reproduced courtesy of Irish, personal communication, September 12, 2016).

Semantic memory was assessed with a schedule that included all AMI and EAMI semantic schedule questions (Appendix G; Appendix K). The EAMI semantic assessment followed the following format (Irish et al., 2008): participants were asked to provide information relating to three distinct categories of information for each life period: (i) Names of people, (ii) Daily Living, and (iii) Important Dates. Each life period was scored from 14 points with exception of the Childhood period (Age 0-5 years; 5-11 years; 11-18 years), for which point subtotals of 10, 10, and 14 points were allocated to each of the three age bands respectively. For Names of People, the provision of three full names and the participant's relationship to each was scored one point for each full name and one point for each relationship (maximum of six points; half points were awarded for providing only christian or surnames). For Daily Living, participants scored one point for naming an institution/association they were involved with at that time, one point for its location, one point for specifying the type of work/study/hobby that was involved, and one point for the means of travel there (maximum of four points). Providing a specific date for an important event was awarded one point for the date, one point for month, one point for year, and one point for location of event (maximum of four points). No points were awarded for repetitions across life periods.

Table 2-5. *End-of-trial EAMI scoring schedule for episodic events. A maximum of 1 point is awarded for each category, based on degree of detail provided.*

Score	Information
	1. Event Detail
1	Producing a framework for a clear, discernible once-off event lasting less than 24 hours
0.5	Vague, once-off event lasting less than 24 hours
0.5	Detailed event lasting longer than 24 hours
0.5	Event that has been repeated (and is likely to be semanticised)
0.5	Skeletal description of an event that requires continual probing for more information
0	No event recalled
	2. Temporal Specificity
1	Year, month, date, specific time of day (provision of 4 temporal elements)
0.5	Provision with specificity of any 2 elements (e.g. year/age, month), guessing or hesitation of other 2 elements
0	Indications of guessing, hesitancy, speculation on 3 elements
	3. Sensory / Perceptual Detail*
1	Clear sensory details relating to the main event; can be visualized by the scorer
0.5	Vague descriptions with absence of details / regularly encountered scenes (semanticised)
0	Indications of no mental imagery (e.g. fact-like descriptions divested of mental imagery; emotional rather than visual recall)
	4. Spatial Detail
1	Recall of general location (allocentric), plus specific location within the spatial array (egocentric)
0.5	Recall of either allocentric or egocentric information but not both
0	No recall or speculative answers
	5. Emotion Detail
1	Clear recall of actual emotions experienced, not over a period of time or speculating about what is 'normally felt'
0	Unable to recall the emotion felt, speculative answers
	6. Thoughts (Meta-cognition)
1	Able to clearly recollect thoughts at the time of the event (separate from feelings)
0	Inability to do so or reiteration of feelings
	7. Implication
1	Recall of specific activities 36 hours before and 36 hours after the main event, without speculation
0.5	Recall of events either before or after the main event but not both, or speculative answers for either
0	No recall of events preceding or subsequent to the main event, or speculative / semanticised answers for both

Note. Each phenomenological category is scored from 1 point, with a maximum of 7 points awarded for each episodic memory. *What is 'seen' in the mind's eye during EM recall. This is typically visual imagery, but may also involve other sense modalities. Acknowledgement: M. Irish (personal communication, September 12, 2016).

Episodic memory testing for each life period comprised three event enquiries following the semantic section except for Childhood, in which one event enquiry followed each Before School, Primary School and High School semantic section. The twelve event

enquiries involved asking participants to describe a personal event with as much detail as possible, relating to one of the following four themes which were rotated across Early Adult Life, Later Adult Life, and Recent Life epochs:

i. a meeting or event linked to a person
ii. a trip or journey
iii. college/professional life or professional life/retirement
iv. a family event or occasion.

These themes bridged the thematic specificity of the AMI and the free recall conditions of the EAMI, allowing AMI-based comparisons to still be drawn between baseline and end-of-trial recall performances. Participants were initially invited to engage in free recall of an event and to describe it with as much detail as possible, which replicated AMI baseline testing conditions. They were offered the prompts (Table 2-4**)** if they struggled to recall any memory at all. Following this free recall phase, the interviewer then probed for presence of contextual details by moving through the EAMI Episodic Subscale Event Details Checklist (adapted from Irish et al. (2011a); Appendix H). Participants were kept reminded of the life period under investigation with cards placed on the table in from of them ('Before you went to school (up to five years old)'; 'Primary school (aged between five and 11)'; 'High school (aged between 11 and 18)'; 'Between 18 and 30'; 'Aged 45 until six years ago'; 'Between six years and twelve months ago').

2.4.4.2 Avoidance of baseline episodic events

At the beginning of each ABM interview, the assessor read an introductory statement that notified participants that they may sometimes begin to describe a memory and then be asked to think of a different memory. This was because, as outlined previously, during the active phase of the Enrichment trial PD-active participants received an intervention that involved elaborating and rehearsing three episodic memories taken from their baseline AMI

autobiographical memory interview. Therefore, to avoid possible scoring advantages gained by the inclusion of rehearsed events, *all* participants (PD-active, PD-passive and HC) were asked to provide a different memory if they gave *any* baseline event spontaneously on the first pass.

For each interview, the assessor was provided with the list of memories a participant had given at AMI baseline testing, which were to be avoided. These 'Avoid Events' were described in truncated paraphrases that captured the central event (Appendix I). The purpose for paraphrasing the baseline events in this way, was to provide the blinded interviewer enough detail to recognise a baseline event, but also keep the format as simplified as possible so that they would be unlikely to identify study arm allocation through the differing presentations between the groups, of the three baseline event items used in elaboration exercises by the PD-active group only (high school event, wedding event, a recent journey).

As outlined previously, during elaboration exercises with the PD Active Enrichment group, three 'substitute' baseline memories were discreetly identified at the earliest occasion, which were destined to replace the elaborated ones at end-of-trial testing. For the PD-active group, the substitute memories were presented beneath the original baseline events in the 'Avoid Events' sheet. For PD-passive group, re-phrased descriptions of the same baseline events were presented underneath in the same manner. To help keep the situation unclear and maintain blinded conditions, the interviewer was not informed of the Enrichment study's memory elaboration exercises or explained the origins of any substitute events, until all end-of-trial testing was completed.

All participants were permitted to resume recall of baseline events if they spontaneously provided these in the first instance and were unable to produce an alternative event when asked to do so. The difference for the PD-active group was that if an elaborated High School, Wedding or Recent Journey baseline event was produced and an alternative

event was not forthcoming, the interviewer cued the participant with the substitute event via graduated disclosure of its three paraphrased descriptor statements. Guidelines for avoidance of events are summarised as follows:

1. If a participant starts to describe any memory listed on the baseline events avoid sheet, they must be asked to think of a different memory because baseline memories are to be avoided wherever possible.
2. The only times participants can use a baseline memory is if they cannot produce an alternative memory.

    2a. Substitute baseline memory events are located underneath Avoid events 1.3, 2.1, 4.2. They can be used if participants bring them up spontaneously; or if participants start to describe an Avoid event but cannot provide a different memory when asked to.

ABM retesting lasted approximately two hours, and all interviews were recorded with consent using an H4N microphone. Baseline measures of ABM using the AMI (Kopelman et al., 1989) were scored after completion of Baseline testing by Nicolson (2016) and the author. At the completion of end-of-trial ABM testing for all participant groups, data was scored using AMI and EAMI testing procedures, by the author. The scoring sheets for semantic and episodic end-of-trial testing are presented in Appendix K.

All end-of-trial episodic events from PD participant groups were transcribed using Dragon Naturally Speaking desktop software and scored following the EAMI scoring protocol. An initial 60 memories from five randomly-selected participants were also scored by a blinded senior researcher from the EAMI development and publication group (Irish, personal communication, October 23, 2017). Regular scoring comparison reviews were held over telephone and email. An intra-class correlation coefficient of 0.897 was achieved with a 95% confidence interval from .828 to .939, F (1, 59) = 9.730, p =.000. This was calculated on

IBM SPSS statistics 25 using a two-way mixed model with absolute agreement. Due to time constraints, episodic events for the HC group were not transcribed. Instead they were scored using audio playback. Twelve PD events were scored off audio and then off transcribed interview for practice comparisons to check maintenance of scoring consistency. Scoring of HC events then took place after completion of scoring of the PD groups, by which time scoring proficiency was accurate and efficient. To check consistency, for every 48 HC events, one randomly selected PD event was scored again using audio, and compared on scores awarded using transcribed material.

Chapter 3: Results

3.1 Demographic and clinical features of the participants

Table 3-1 summarizes the demographic, clinical characteristics, and global scores of the PD-active, PD-passive, and HC participants at the screening assessment prior to trial commencement. Detailed information on neuropsychological testing will be included in a forthcoming PhD thesis (Megan Livingstone). The PD group achieved marginally but significantly worse MoCA scores than the HC group, and higher HADS depression and anxiety measures (Table 3-1). The two PD groups had equal risk scores for progression to PD-MCI. The component z-score measures were used to generate the risk score were significantly worse in the PD group than the HC group for TEA Map Search (1 min: PD-active: 0.02±1.11; PD-passive: -0.16±0.77; HC: 1.00±0.79), Stroop Interference (PD-active: 0.24±0.94; PD Passive: 0.09±0.93; HC: 0.82±0.69), and Trails B (PD-active: 0.45±0.91; PD-passive: 0.22±1.19; HC: 0.84±0.86). The two PD groups did not differ on any cognitive or neuropsychiatric measures. Moreover, none of the PD patients met the NZBRI level II PD-MCI criteria (data produced courtesy of M. Livingstone, J. Goh, M. Goulden, D. Myall, T. Anderson, L. Hale, H. Mulligan, J. Dalrymple-Alford; New Zealand Brain Research Institute; University of Canterbury; Otago University). Four HC participants were lost to attrition at end-of-trial ABM assessment (two females, two males); and three at end-of-trial ToM assessment (two females, one male).

Table 3-1. *Clinical, cognitive and psychiatric measures of PD and HC participants at baseline (M±SD).*

	Group			**Difference of means**	
	PD-active	PD-passive	HC	HC : PD	PD-A : PD-P
Demographic Characteristics					
Sex; M:F	13:8	13:6	15:13	-	-
Age	69.4±6.8	69.5±5.3	73.2±6.5	-	-
Education	13.0	12.9	13.4	-	-
Clinical Measures					
PD Symptom duration (yrs) at screening	7.90±5.81	7.57±4.66	-	-	-.34
PD Hoehn & Yahr	2.24	2.08	-	-	-.16
HADS Anxiety	4.57±3.41	4.42±2.61	2.89±3.15	-1.62*	-.18
HADS Depression	3.62±2.40	3.79±3.07	1.93±2.31	-1.69*	.34
MoCA (raw score)	26.10±2.07	25.47±2.14	27.61±1.6	1.81**	-.62
Risk Score for future MCI	0.34±0.22	0.39±0.23	-	-	-

Note. Difference is significant at * $p < .05$; ** $p < .001$, based on independent samples t tests comparing groups at baseline. Risk Score for future MCI = the probability of advancing to PD-MCI status over the next four years based on age, MoCA, TEA Map Search, Stroop, and Trails B. *Abbreviations:* HADS = Hospital Anxiety Depression Scale; MCI = Mild Cognitive Impairment; MoCA = Montreal Cognitive Assessment; PD = Parkinson's disease; PD-A = PD-active group; PD-P = PD-passive group.

3.2 Theory of mind

This analysis was generated using ANOVA applied to a multi-level linear model. The main analysis used Group (HC; PD-active; PD-passive) as three levels of the between-group factor, and Trial (baseline vs end-of-trial) as the repeated measures factor. An additional covariate analysis included education, age at study entry and sex.

To re-cap, the ToM card sorting task used 16 short story sequences to compare group performance on a "false belief" condition and three non-ToM control conditions. The latter conditions examined sequencing errors caused by factors other than false belief ToM.

The mean scores for the four conditions for each of the three participant groups, across baseline and end-of trial are shown in (Figure 3.1). The "mechanical" and "social script" scores were higher in all groups compared to the "capture" and "false belief" scores.

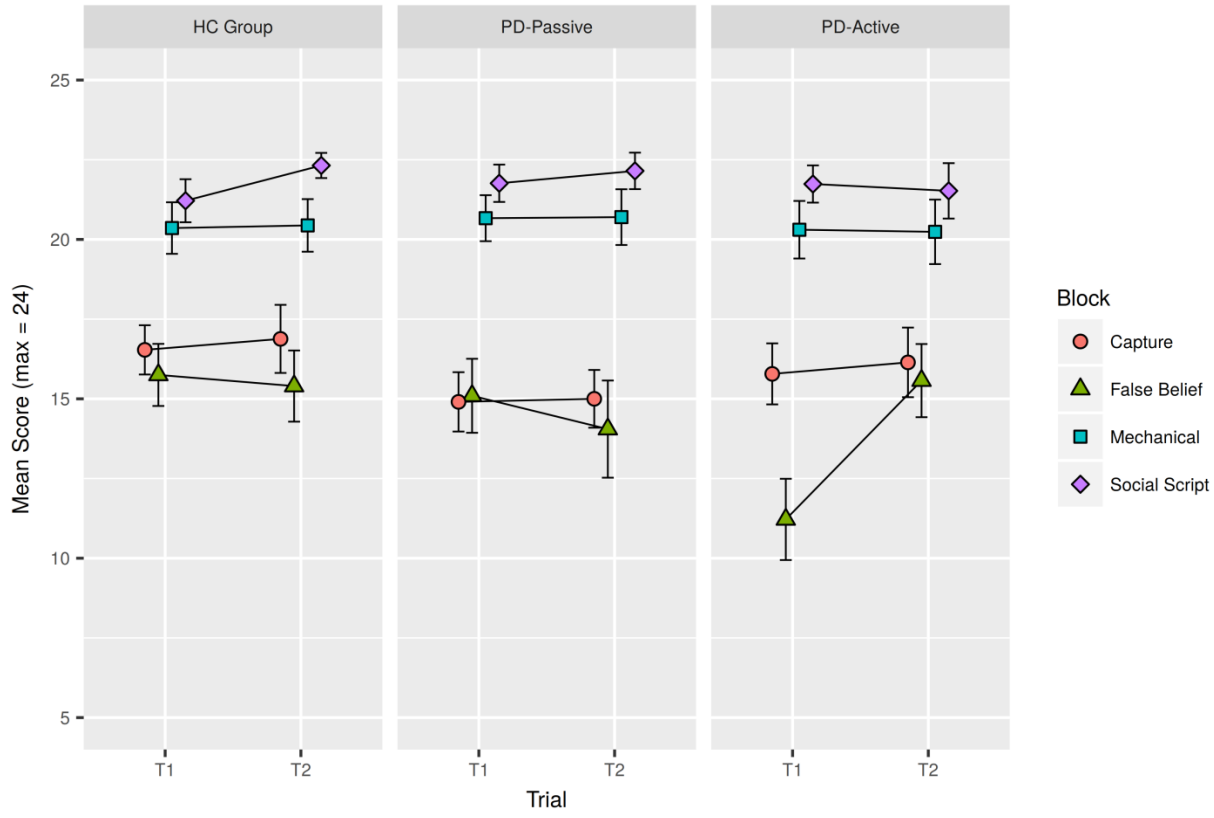


Figure 3.1. Mean baseline and end of trial ToM scores for HC, PD-active and PD-passive participant groups across conditions(Langdon et al., 1997). *Abbreviations*: HC = Healthy controls; PD = Parkinson's disease.

Performance in the ToM false belief condition did not differ across the three groups, Group main effect, F (2, 65) = 1.08, $p > 0.1$. There was also no difference in performance between baseline and end-of-trial, Trial main effect, F (1, 62) = 1.55, $p > 0.1$; Figure 3.1. There was however a Group x Trial interaction effect, F (2, 62) = 6.15, $p < .01$, with the PD-active group showing poorer scores at baseline and an increase by end-of-trial. This was confirmed using a Tukey post-hoc test in that group, $p < 0.02$. Inclusion of Education, Sex and Age covariates did not change this significant interaction effect, Group x Trial, F (2, 61) = 6.55, $p < 0.01$; Age, Sex, Education, all $p > 0.1$.

For the three other (control) conditions, all groups performed similarly overall and across baseline and end-of-trial, with no interaction effects observed. Social Script: Group, F (2, 65) < 1.0, $p > 0.1$, Trial F (1, 62) < 1.0, $p > 0.1$**,** Group x Trial F (2, 62) = 1.23, $p > 0.1$;

Mechanical: Group F (2, 65) < 1.0, p > 0.1, Trial F (1, 62) < 1.0, p > 0.1**,** Group x Trial F (2, 62) < 1.0, p > 0.1**;** Capture: Group F (2, 65) < 1.0, p > 0.1**,** Trial F (1, 62) < 1.0, p > 0.1, Group x Trial F (2, 62) < 1.0, p > 0.1.

3.3 Autobiographical memory

A multi-level linear model was again used here. In this instance, the ANOVA for AMI data used Group (HC; PD-active; PD-passive) as three levels of the between-group factor, and Epoch (e.g. three life periods for the AMI) and Trial (baseline versus end-of-trial) as the repeated measures factors. An additional covariate analysis included education, age at study entry and sex. Follow-up analyses examined (a) HC group versus All PDs and (b) just the two PD groups. This analytic procedure was conducted for episodic memory scores and for semantic memory scores for the AMI. As the EAMI was conducted only at end-of-trial, the same procedures were used but the Trial factor was not relevant. For the EAMI, there were four life periods (4 levels for Epoch).

3.3.1 Semantic memory

3.3.1.1 AMI semantic memory: pre vs. post-trial

To recap, the AMI semantic memory schedule examined performance of semantic recall over three life periods, Childhood (ages 0-18), Early Adulthood (ages 18-30) and Recent Life. The baseline AMI Recent Life period examined the five years preceding test date. At end-of-trial, and to avoid memories relating to the Enrichment Study, the timeframe for AMI Recent Life period encompassed the previous six years, and excluding the twelve months preceding the test date for five questions. Each time period was scored from a total of 21 points, which was converted to a percentage of maximum possible score for each participant. The percent mean semantic memory scores for the AMI in the three groups across Epoch, both at baseline and end-of-trial, are presented in Figure 3.2. Superior semantic recall was evident in the HC

group, Group main effect, F (2, 61) = 6.56, p < 0.01; irrespective of Trial, Group x Trial, F (2, 61) < 1.0, p > 0.1); or life period, Group x Epoch, F (4, 244) = 1.58, p > 0.1; Group x Epoch x Trial, F (4, 244) = 1.36, p > 0.1.

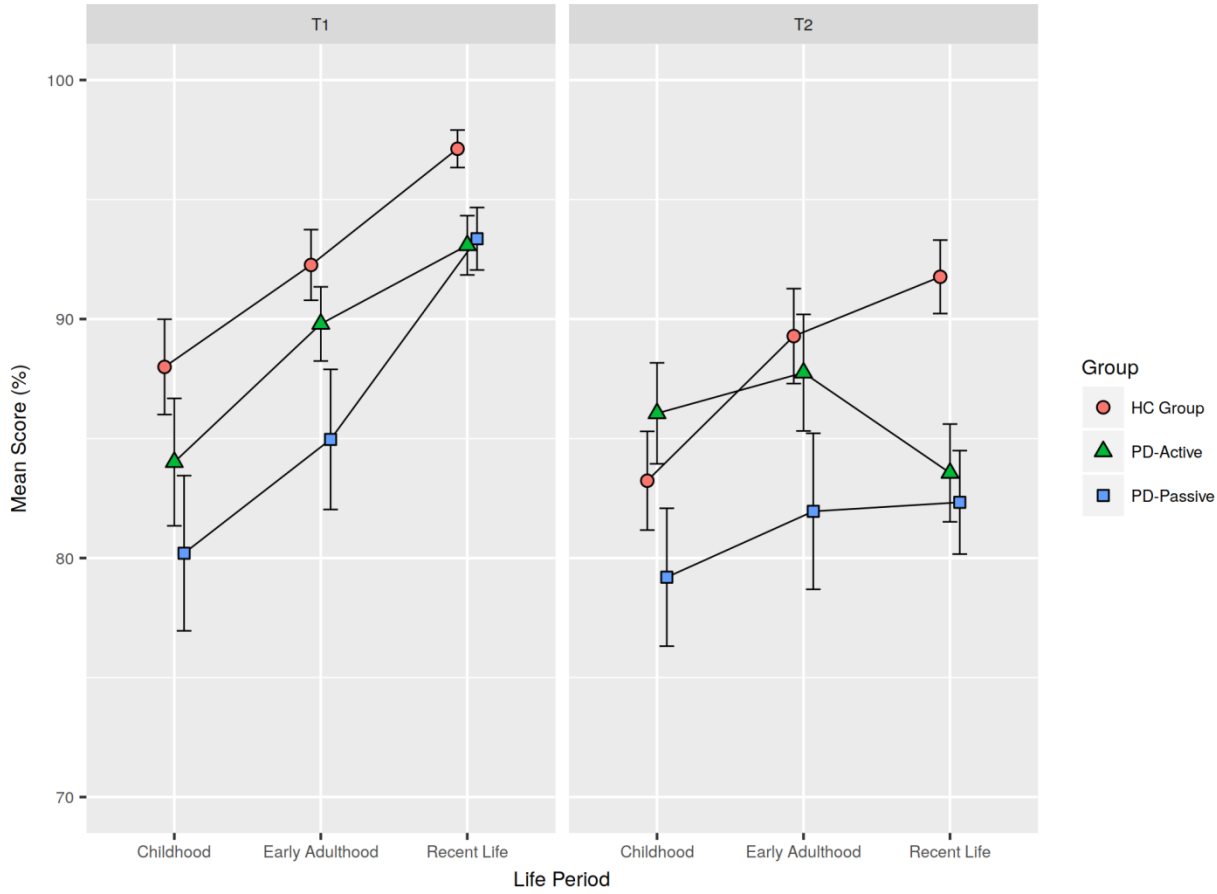


Figure 3.2. Baseline and end-of-trial AMI semantic memory scores for the HC, PD-passive and PD-active groups across life periods. *Abbreviations:* HC = Healthy controls; PD = Parkinson's disease; T1 = Trial 1 (baseline), T2 = Trial 2 (end-of-trial).

Post-hoc contrasts (Tukey) confirmed higher semantic memory scores of the HC group compared to the PD-passive group, p <.01. The PD-active group had intermediate semantic recall and did not differ from either the HC group or the PD-passive group (p > 0.5). The main effect of Group remained after controlling for demographic covariates, Group F (2, 58) = 6.31, p < 0.01; Age, Sex, Education, all p > 0.1. Semantic scores showed a recency effect with highest scores for Recent Life and lowest scores for Childhood, Epoch main effect, F (2, 244) = 20.42, p < 0.001. However, semantic memory scores were lower at end-

of-trial than at baseline, Trial main effect, F (1, 61) = 22.45, p < 0.001**.** The only other effect was an Epoch x Trial interaction effect, F (2, 244 = 5.98 p < 0.01; Figure 3.3. Baseline and end-of-trial AMI semantic scores for each life period examined, collapsed across groups). That is, regardless of group, end-of-trial AMI semantic recall remained relatively stable for Childhood and Early Adulthood life periods compared to baseline, but was more clearly poorer at end-of-trial for the Recent Life period. There was no Group x Trial interaction, F (2, 61) < 1.0, p > 0.1, or Group x Epoch x Trial interaction, F (4, 244) = 1.36, p > 0.1.

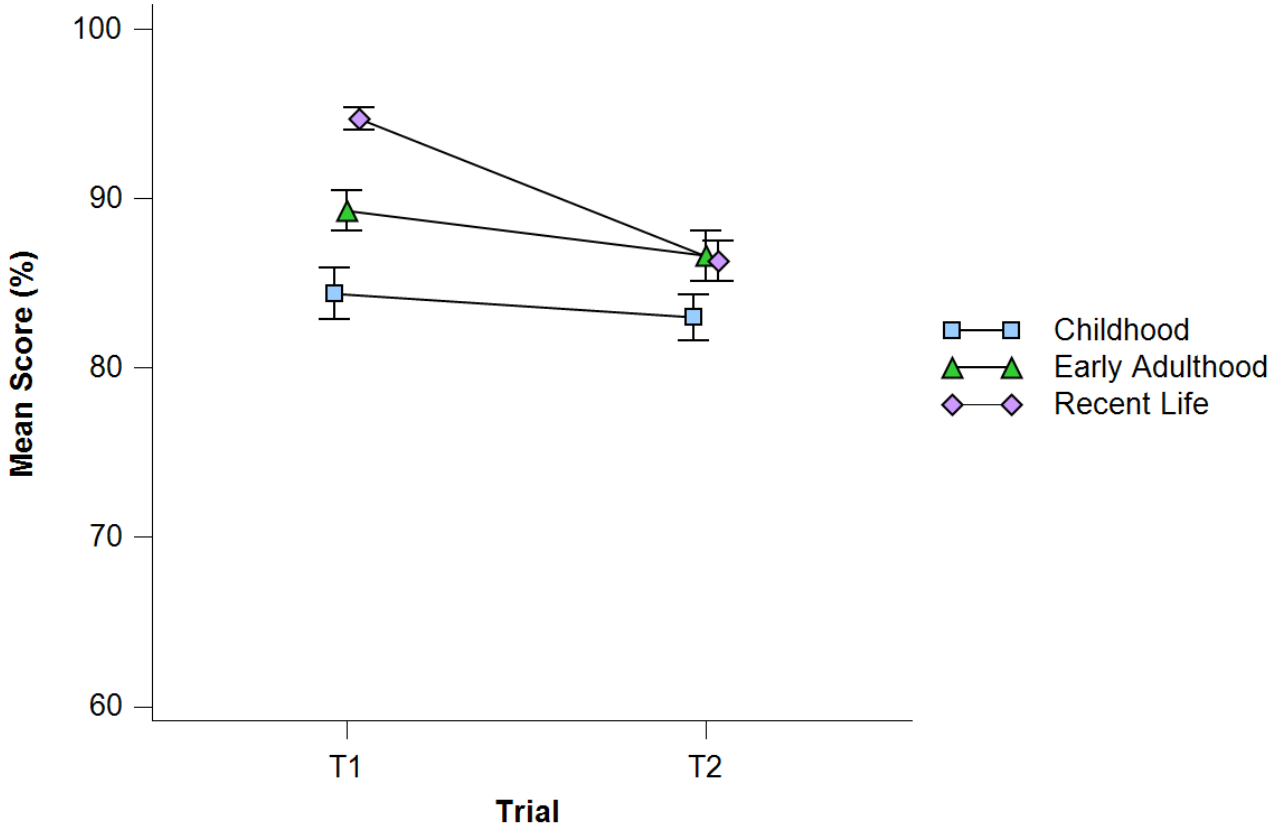


Figure 3.3. Baseline and end-of-trial AMI semantic scores for each life period examined, collapsed across groups. *Abbreviations:* T1 = Trial 1 (baseline), T2 = Trial 2 (end-of-trial).

Comparison of the HC group vs All PDs (the two PD groups combined) repeated the Group main effect for semantic recall, F (1, 62) = 8.82, p < 0.01. Similarly, there was a main effect for Epoch, F (2, 248) = 20.41, p < .0001, Trial, F (1, 62) = 22.45, p < .0001, Epoch x Trial, F (2,248) = 5.98, p < .01. In this instance (HC vs all PD), the Group x Epoch x Trial

interaction just failed to reach significance, F (2, 248) = 2.65, p = .07. No other HC Group x All PD group effects were found, Group x Epoch, F (2, 248) = 1.06, p > 0.1; Group x Trial, F (1, 62) < 1.0, p > 0.1. Separate analysis restricted to the two PD groups confirmed no main effect, F (1, 38) < 1.0, p > 0.1; and in particular no PD-Group x Trial interaction, F (1, 38) < 0.1, p > 0.1; or PD-Group x Epoch interaction, F (2, 150) = 1.01, p > 0.1, on the AMI semantic memory score.

3.3.1.2 EAMI semantic memory: post-trial

The EAMI life periods overlapped with the AMI, but it also included a fourth life period, Later Adulthood (age 45 to 6 years ago). Like the AMI, each life period contained three events. End-of-trial performance between the three groups on the EAMI semantic subscale showed a significant main effect for Epoch, F (3, 183) = 18.99, p < 0.001, with semantic recall scores showing a mild increase from Childhood to Adulthood, but then decreasing for the Recent Life period (Figure 3.4A). Non-significant values were returned for the Group effect, F (2, 61) = 2.25, p > 0.1, and the Group x Epoch interaction effects, F (6, 183) = 1.90, p > 0.1. However, a Group main effect approached significance when the HC Group was compared with All PD combined, F (1, 62) = 3.52, p < .07, and a Group x Epoch interaction effect also emerged, F (3, 186) = 3.61, p < .05. The latter interaction reflected poorer semantic recall for Later Adulthood and especially the most recent period for All PD compared to the HC group (Figure 3.4B). This interaction effect remained when controlling for Age, Sex and Education, F (3, 186) = 3.61, p < .05; Age, Sex, Education, all p > 0.1.

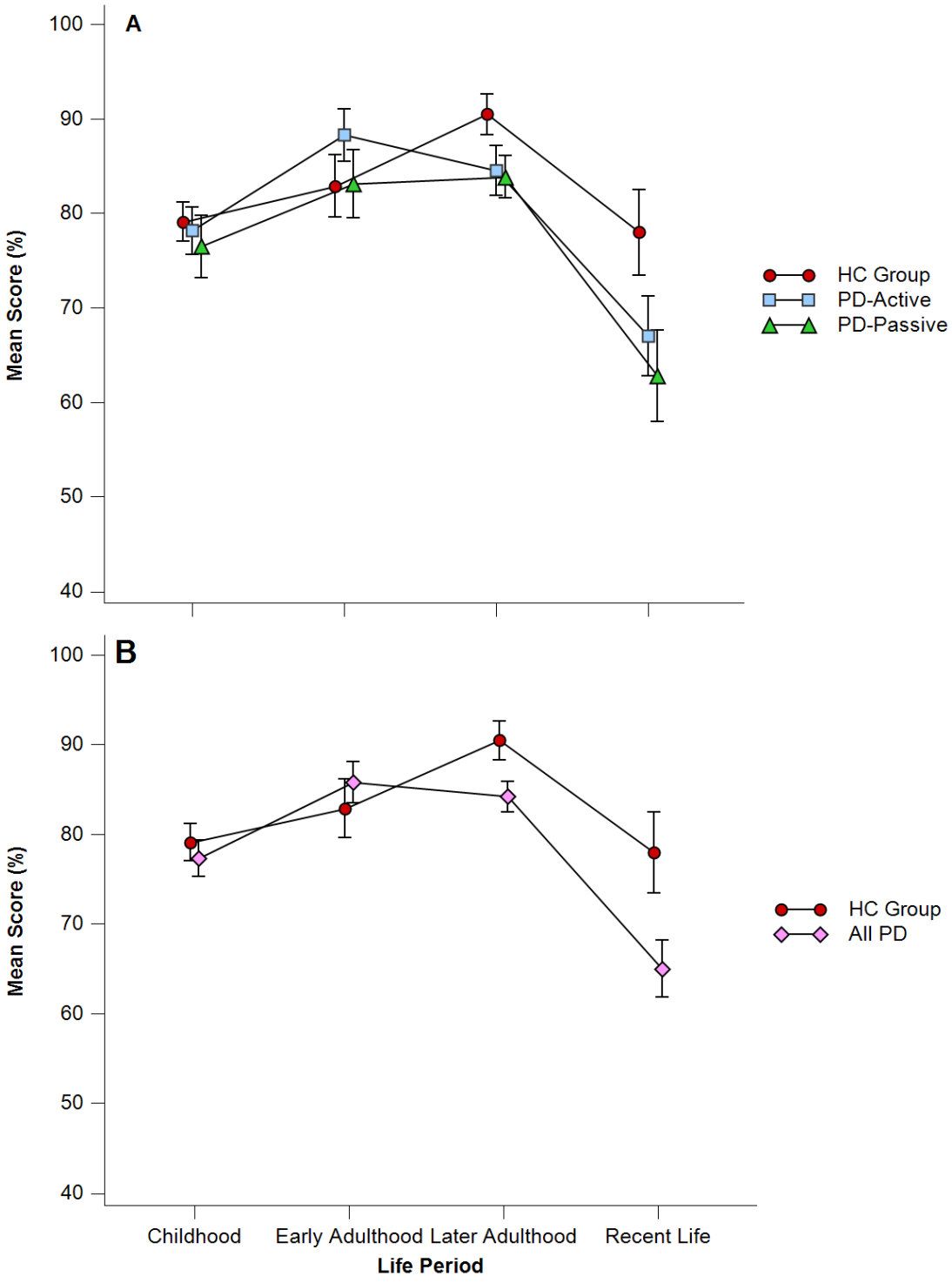


Figure 3.4. End-of-Trial EAMI mean semantic scores across life periods for A) PD-active, PD-passive and HC groups; and B) HC and All PD groups. The maximum score for Childhood is 34 points per participant (Before School = 10 points; Primary School = 10 points; High School = 14 points). The maximum score for all other life periods is 14 points per participant. *Abbreviations:* HC = Healthy control, PD = Parkinson's disease.

3.3.1.3 EAMI semantic memory: post-trial Childhood life period sub-analysis

The three age periods of the EAMI Childhood period were subjected to a sub-analysis to more closely scrutinize semantic recall between ages 0-5 (before school), ages 5-11 (primary school), and 11-18 (high school). Group performance of the two PD groups and HC group are presented in Figure 3.5. There were no differences in performance between the HC, PD-active and PD-passive groups, F (2, 61) < 1.0, p > 0.1; or any change in performance across Epoch, F (2, 122) = 1.22, p > 0.1; or Group x Epoch interaction effect, F (4, 122) < 1.0, p > 0.1. These findings were replicated when comparing All PD vs HC Group, F (1, 62) <1.0, p > 0.1; Epoch, F (2, 124) = 1.23, p > 0.1; Group x Epoch, F (2, 124) < 1.0, p > 0.1).

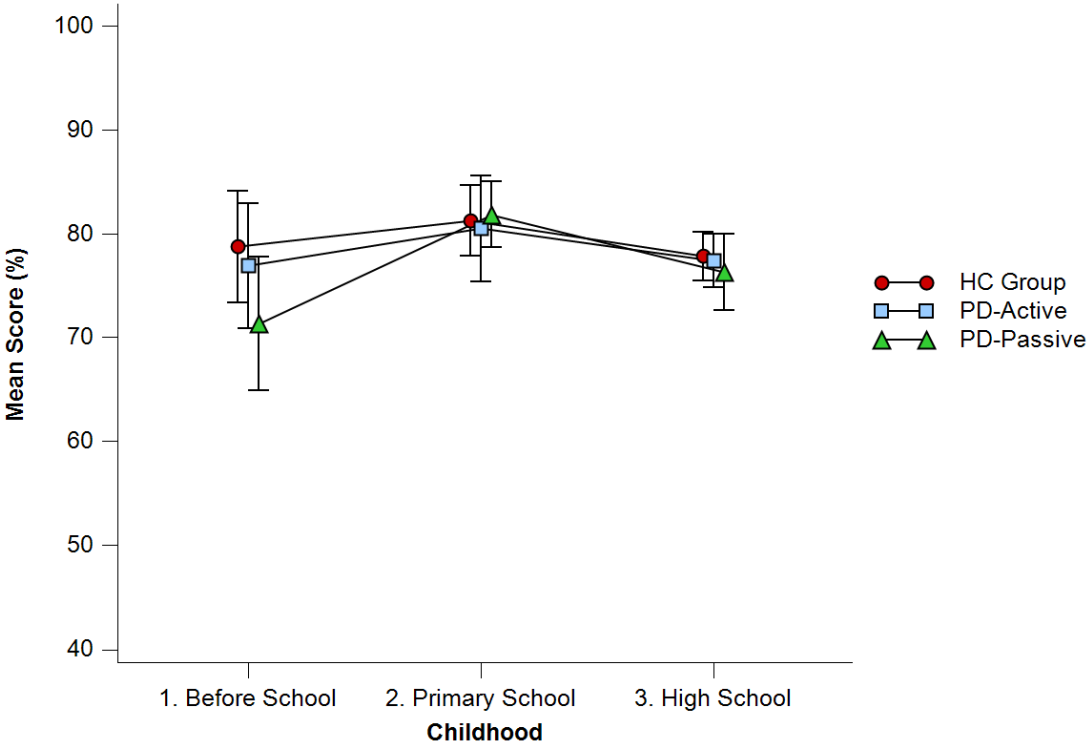


Figure 3.5. End-of-trial EAMI semantic scores for PD-active, PD-passive and HC groups across the Childhood life period. Before School and Primary School sub-periods are scored from a maximum of ten points, and High School from 14 points per participant. *Abbreviations:* HC = Healthy control; PD = Parkinson's disease.

3.3.2 Episodic memory

The AMI was used as a measure of baseline and end-of-trial episodic memory performance. To recap, the AMI episodic schedule examined performance of episodic recall over three life

periods, Childhood (ages 0-18), Early Adulthood (ages 18-30) and Recent Life (within the last five-to-six years). Three episodic events were allocated to each life period. Each event was scored from three points, and thus each life period in the AMI was scored from a maximum of nine points. The EAMI was used as a second measure of end-of-trial episodic memory to investigate the presence of sensory-perceptual and other contextual details associated with episodic memory and autonoesis. With the EAMI, however, each event was scored from a maximum of 7 points, so that each life period in the EAMI was scored from a maximum of 21 points. To simplify comparisons, event scores for both the AMI and EAMI schedules were converted to percentages for all episodic (and semantic) baseline and end-of-trial analyses.

3.3.2.1 Criteria and selection of episodic memories

Post-trial AMI and EAMI episodic memory scores were analysed using two methods. The first method included all episodic ABMs collected at end-of-trial and is the main analysis referred to in the body of these results. Another analysis exclusively examined episodic memories that were different to the memories provided at baseline.

The main analysis, which includes all episodic memories reported regardless of whether they were elicited previously at baseline, excluded for the PD-active group the three memories per participant that had been elaborated during the trial (Table 3-2). These excluded memories could not be used because, as rehearsed memories, they could have conferred a scoring advantage to the PD-active group. Of the PD-active group, there were two participants who spontaneously produced three memories at end-of-trial that had been elaborated during the trial, and which were identified by the "blind" interviewer via reference to the 'Event Avoid' sheet. On each of these three occasions the participants were explicitly asked to report a different memory, but they could not. Therefore, the elaborated memories

were substituted with unrehearsed ‘replacement baseline’ memories gathered during the earliest memory elaboration sessions.

3.3.2.2 Missing episodic values

For the main results, there were some missing episodic memory scores in the end-of-trial Childhood life period. For one PD-passive group participant, two of the three Childhood period events (event 1.1., event 1.2.) were not requested by the “blind” interviewer. This person’s Childhood period score was designated as a ‘missing’ value, rather than using the single event obtained (event 1.3., age 11-18), because differences in memories recalled across the three Childhood sub-periods (before school, primary school, high school) were deemed as potentially too variable.

For one PD-active group participant, event 1.3 (high school) could not be included for end-of-trial analysis because it had been a baseline ‘elaboration’ memory and was therefore to be avoided. The mean Childhood period score for this PD participant was therefore also re-designated as a ‘missing’ value. For the same participant, a second event (2.1.), from the Early Adulthood period, was also excluded because it was an elaborated baseline event. In this instance, however, the participant’s Early Adulthood period total was calculated as the mean of the two remaining events (events 2.2., 2.3.). These small variations in sample cell size could be accommodated by the multi-level linear model used for analyses.

3.3.2.3 Treatment of episodic data

The following results also include three memories from two participants in the PD-active group that are ‘replacement baseline’ events. On each of these occasions, participants initially produced a memory from baseline that was elaborated during the trial, but they were unable to generate an alternative memory independently when asked to do so. To reiterate, if participants gave a baseline memory on the first pass, it would be identified quickly by the

interviewer via reference to the Avoid Events sheet. Participants would then be explicitly asked to think of an alternative memory. If they could not, investigation of the baseline memory was resumed. For PD-active participants however, if these same initial circumstances involved elaborated baseline events (1.3, 2.1, 4.3), resumption of the 'baseline' memory would instead use an unrehearsed 'replacement baseline' memory. Therefore, there are three of these substitute memories in the PD-active episodic data values set. The analysis also includes 23 events that were awarded zero scores on both AMI and EAMI end-of-trial measures, because participants failed to generate any memory at all. A summary of data treatment is presented in Table 3-2.

Table 3-2. *Organisation of end-of-trial AMI and EAMI episodic memory data. Letters represent different types of data treatment across life periods and participant groups.*

	Childhood (Ages 0 - 18)			**Early Adulthood** (Ages 18 - 30)			**Later Adulthood** (Age 45 – > last 6 yrs)			**Recent Life** (< last six yrs)			**Total Events**	
	1.1	1.2	**1.3**	**2.1**	2.2	2.3	3.1	3.2	3.3	4.1	**4.2**	4.3	AMI	EAMI
HC *n* = 24	*e e* *e e* *f f* *f f*				*e e*						*f*		216	288
PD-active *n* = 21	*e f* *f*	*e e*	*a d* *d f* *f*	*b d* *e f*	*f f* f^1 f^1	*e* f^1				*e e* f^1 f^1	*e*	*e e* f^1	189	252
PD-passive *n* = 19	*c e* *f* f^1	*c f* *f*	*f f* f^1 f^1 f^1 f^1	*e e* f^1 f^1 f^1 f^1 f^1	*e*					*e e*	*e* f^1		171	228
Event *n*	192			192			192			192			576	768

Note. AMI baseline and end-of-trial episodic analyses were based on Childhood, Early Adulthood and Recent Life periods only. EAMI end-of-trial analyses also include the Later Adulthood life period (shaded). *a* = 1 event excluded from post-trial analyses because it was a baseline event used in memory elaboration sessions. This event's Childhood period score was re-assigned 'Missing' for post-trial AMI and EAMI analyses. For Childhood period post-trial sub-analyses, events 1.1., 1.2. were reinstated. *b* = 1 event excluded from post-trial analyses because it was a baseline event used in memory elaboration sessions. This event's Early Adulthood life period score was calculated using the mean percentage score of the two remaining events. *c* = 2 baseline memories provided by the same participant that could not be scored as they were not investigated. This Childhood epoch was re-designated a 'Missing' value. (For Childhood life period post-trial sub-analysis, event 1.3. was reinstated). *d* = 3 'replacement' baseline events that were used because an elaborated event was spontaneously provided, and the participant could not think of an alternative memory. e = 23 events across 18 participants, who failed to recall any memories and were awarded zero scores across AMI and EAMI (*n* = 6 HC / *n* = 8 PD-active / *n* = 4 PD-passive). *f* = 34 baseline events included in the main analysis at end-of-trial. For 17 of these events (HC = 5, PD-active = 7, PD-passive = 5), participants were explicitly asked to think of an alternative event but could not. For 17 of these events (f^1; PD-active = 6, PD-passive = 11), participants were not explicitly asked to think of an alternative event (administrative error). Bolded events 1.3, 2.1, 4.2. = memory elaboration baseline events. *Abbreviations*: AMI = Autobiographical Memory Interview; EAMI = Episodic Autobiographical Memory Interview; HC =Healthy control, PD = Parkinson's disease.

3.3.2.4 AMI episodic memory: pre vs. post-trial

The percent mean episodic memory scores for the AMI in the three groups across life periods, both at baseline and at end-of-trial, are shown in Figure 3.6. Superior recall was evident in the HC group with a Group main effect, F (2, 61) = 6.19, $p < 0.01$; irrespective of trial, Group x Trial, F (2, 61) < 1.0, $p > 0.1$); or life period, Group x Epoch, F (4, 242) < 1.0, $p > 0.1$; Group x Epoch x Trial, F (4, 242) < 1.0; $p > 0.1$. Although years of Education were related to performance (F (1, 58) = 6.80, $p < 0.05$, the main effect of Group remained when covariates were included, F (2, 58) = 6.74, $p < 0.01$; Sex and Age, both $p > 0.1$. Pairwise

contrasts (Tukey) confirmed that the HC group had better episodic memory recall on the AMI than both the PD-active group ($p < 0.02$) and the PD-passive group ($p < 0.01$); HC vs All PD, F (1, 62) = 12.48, $p < 0.001$). However, between HC and All PD, there was no main effect for Trial, F (1, 62) = .72, $p > 0.1$; or Epoch, F (2, 246) = 1.07, $p > 0.1$. Separate analysis restricted to the two PD groups confirmed no PD-Group main effect, F (1, 38) < 1.0, $p > 0.1$; and in particular no PD-Group x Trial interaction on the AMI episodic memory score, F (1, 38) < 1.0, $p > 0.1$.

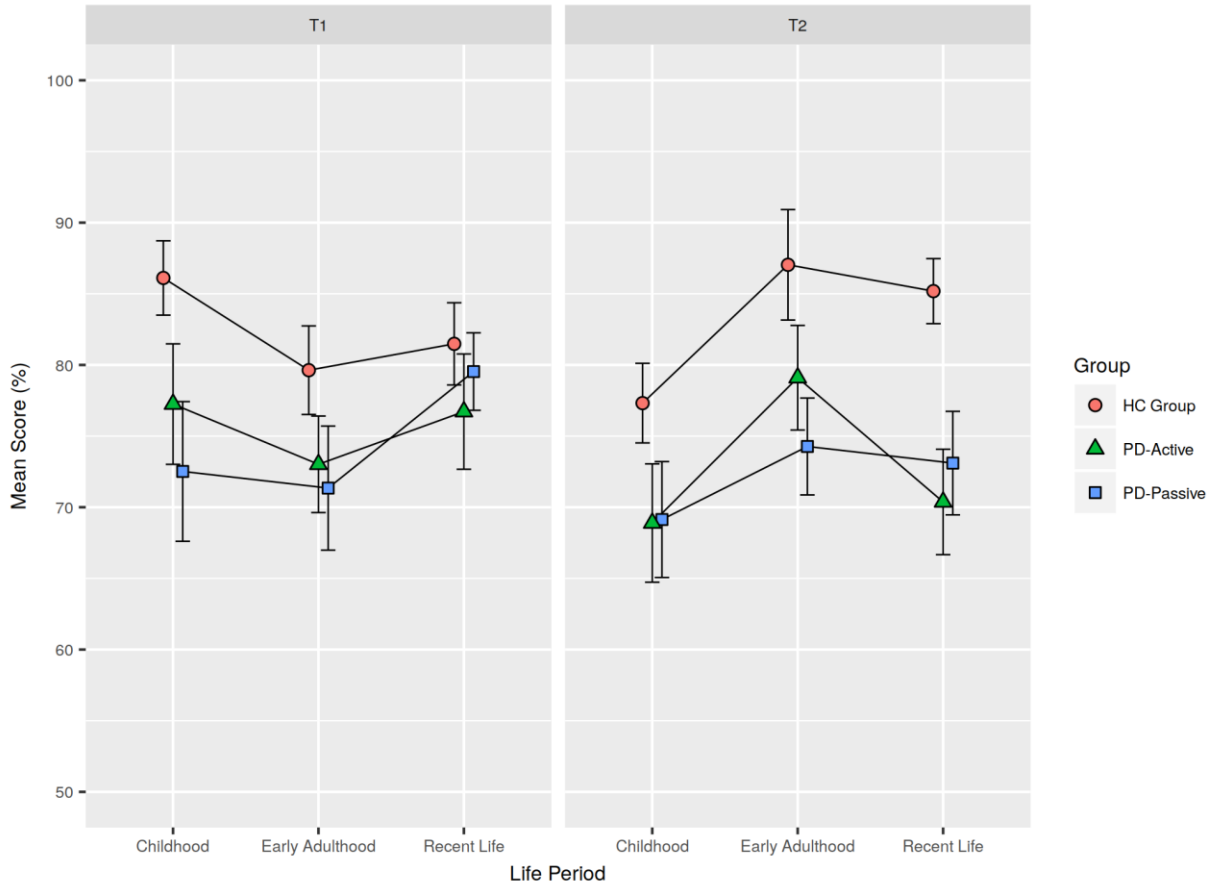


Figure 3.6. Baseline and end-of-trial AMI episodic memory scores for PD-active, PD-passive and HC groups across life periods. Each life period was typically scored from a maximum of nine points per participant (three events per life period). *Abbreviations:* T1 = Trial 1; T2 = Trial 2 (end-of-trial).

The only other effect in the main analysis was an Epoch x Trial interaction, F (2, 242) = 6.76, $p < 0.01$, which was replicated in the analysis for HC vs All PD, F (2, 246) = 6.78, $p < 0.01$; and for the two PD groups, F (2, 150) = 3.73, $p < 0.05$. When each life period was compared between baseline and end-of-trial, combined across all participants, AMI episodic

memory recall at end of trial showed a clear decrease for the Childhood period (0 – 18 yrs), showed a mild increase for Early Adulthood period (18 – 30yrs) and a mild decrease for Recent Life period (last 5 yrs at baseline and 6 yrs to one year ago at end-of-trial; Figure 3.7).

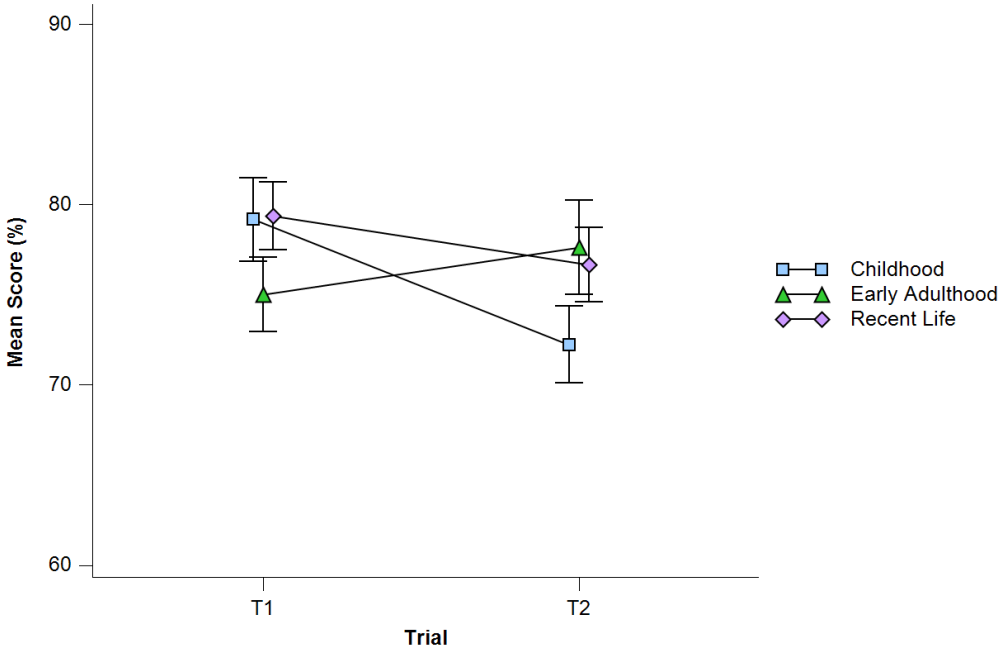


Figure 3.7. Baseline and end-of-trial AMI episodic memory recall collapsed across groups, analysed with all event memories included. *Abbreviations*: T1 = Trial 1 (baseline), T2 = Trial 2 (end-of-trial).

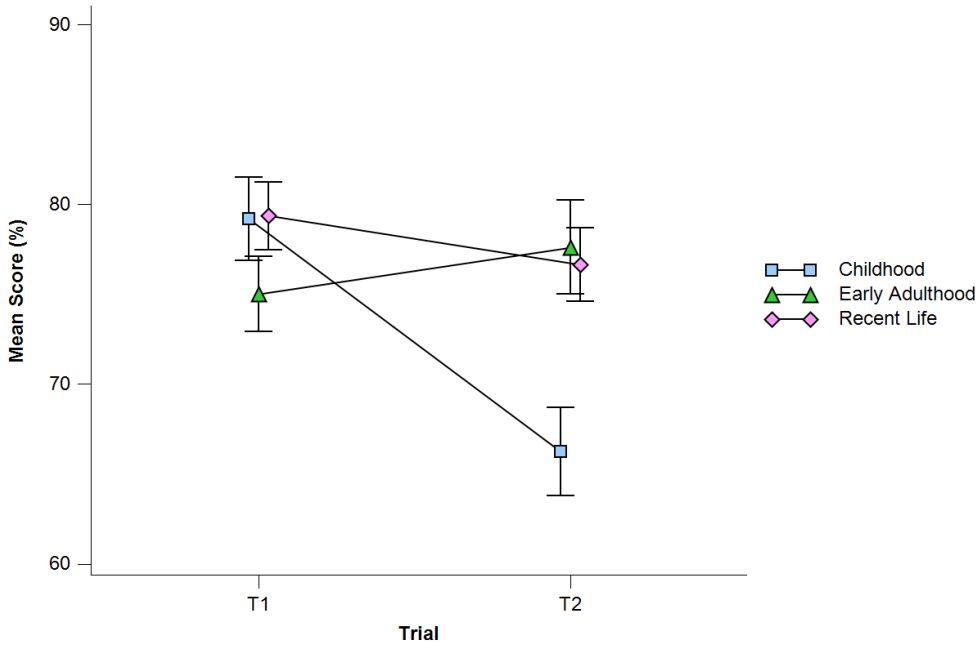


Figure 3.8. Baseline and end-of-trial AMI event memory recall collapsed across groups, analysed with only non-baseline memories. *Abbreviations*: T1 = Trial 1 (baseline), T2 = Trial 2 (end-of-trial).

Figure 3.8 shows the results of an analysis which is restricted only to episodic memories for events *not* given previously at baseline (described in Appendix J). That is, these events were spontaneously provided on the first request by the examiner, or were provided after participants were asked to give a different memory (Table 3-2). For this analysis (of only memories that were different to baseline), recall for Early Adulthood and Recent Life was relatively stable between baseline and end-of-trial. By contrast, there was significantly poorer recall for Childhood at end-of-trial, Epoch x Trial F (2, 243) = 9.71, $p < 0.0001$; Trial F (1, 61) = 5.11, $p < .05$; Epoch F (2, 243) = 4.45, $p < .05$). When Figure 3.8 is compared with Figure 3.7, the childhood drop for end-of-trial versus baseline is clearer and suggests that fewer memory examples from childhood are available, such that a focus on only non-repeated items exacerbates childhood recall at the end of testing.

3.3.2.5 EAMI episodic memory: post-trial

For the EAMI, which was only conducted at end-of-trial, the HC group again showed superior recall, Group main effect, F (2, 61) = 5.13, $p < 0.01$, with no difference between the PD-active and PD-passive groups, F (1, 38) < 1.0; Figure 3.9**).** There was, however, clear evidence of a very strong Epoch main effect for the EAMI, F (3, 181) = 28.93, $p < 0.0001$, irrespective of group, Group x Epoch, F (6, 181) = 1.28, $p > 0.1$. Again, Education was related to recall, F (1, 58) = 4.54, $p < 0.05$, but inclusion of education, age and sex covariates did not change the Group main effect, F (2, 58) = 5.31, $p < 0.01$; Age and Sex, all $p > 0.1$.

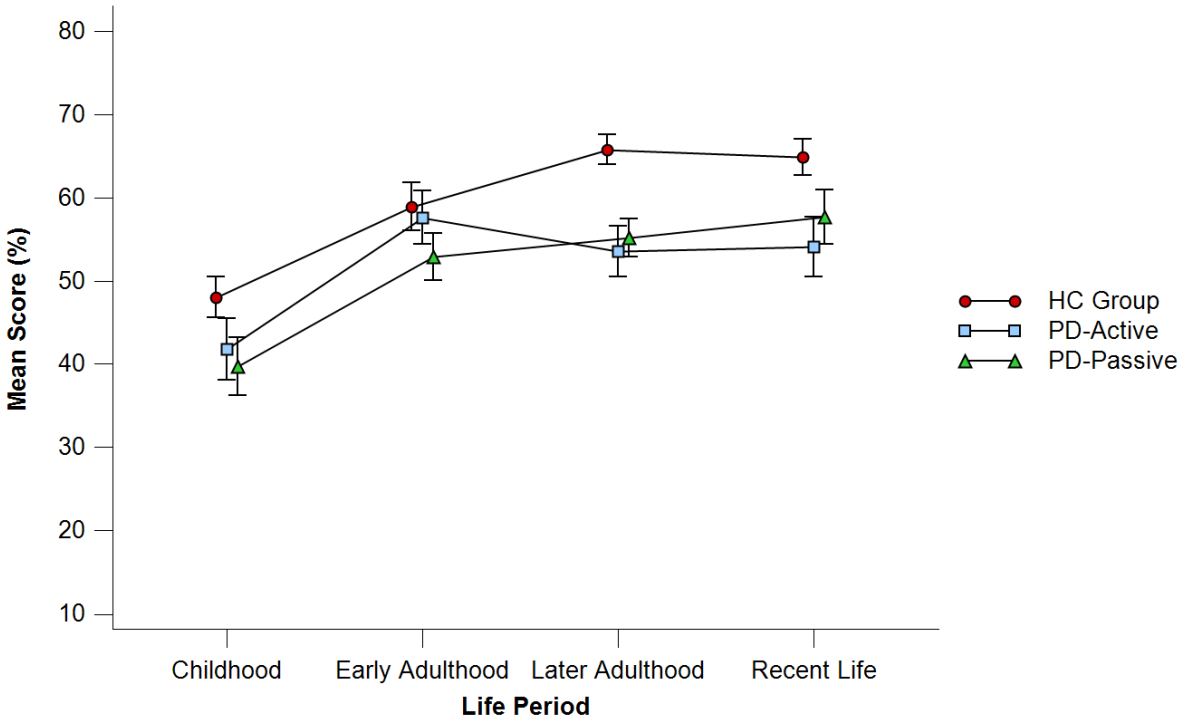


Figure 3.9. End-of-trial EAMI episodic scores across life periods for PD-active, PD-passive and HC groups. Each life period was typically scored from a maximum of 21 points per participant (three events per life period). *Abbreviations:* HC = Healthy control, PD = Parkinson's disease

3.3.2.6 EAMI episodic memory: post-trial Childhood life period sub-analysis

As shown in Figure 3.10, closer examination of Childhood EAMI scores revealed no difference between the three groups for very early childhood (0 – 5 yrs), but no improvement in the PD patients with age during the Childhood period, whereas the HC group produced superior recall for middle (5 – 11yrs) and late (11 – 18 yrs) childhood. This pattern was supported by a significant Group x Epoch interaction across the Childhood sub-epochs, F (2, 121) = 3.07, $p < 0.05$); this interaction survived adjustment for covariates ($p < 0.05$).

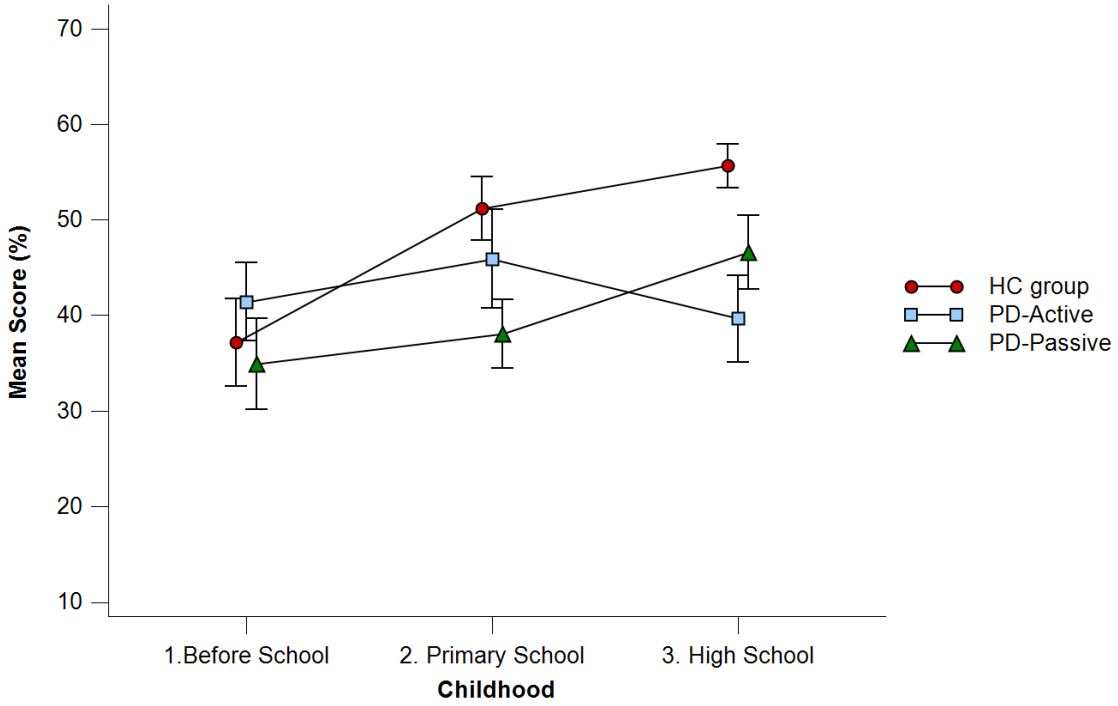


Figure 3.10. EAMI mean episodic scores across Childhood for PD-active, PD-passive and HC groups at end-of-trial. Each sub-period was scored from a maximum 7 points per participant (one event per sub-period). *Abbreviations:* HC = Healthy controls; PD = Parkinson's disease.

Chapter 4: Discussion

The aim of the current study was to investigate the effects of a combined cognitive and physical intervention package on autobiographical memory and cognitive theory of mind, in Parkinson's disease participants. Participants were randomized into intervention (PD-active) and control arms (PD-passive), stratified on the basis of risk of progression to MCI over the next four years. Their performance was compared with age, sex and education-matched HC participants.

4.1 Theory of Mind

Cognitive theory of mind was examined with a card sorting task (Langdon et al., 1997) at baseline and end-of-trial. Overall, PD participants performed similarly to the HC group. However, the PD-active group performed more poorly at baseline than the PD-passive and HC group in the False Belief condition, but improved on this measure at end-of-trial to match the performance of the other two groups. No differences were found between groups on all other conditions. Comparability with the level and pattern of scores reported by Mengelbert and Siegert (2003) and the current data for the three control conditions support the reliability of the current findings. The Mechanical and Social Script conditions yielded similar high scores in all groups, and performance in the more challenging Capture condition was on par with False Belief mean group scores.

Studies to date in cognitive ToM have reported impairments in non-dementing PD participants when compared with controls (Kawamura and Koyama, 2007; Mengelbert and Siegert, 2003; Roca et al., 2000; Salzman et al., 2000). In the current analysis, only the poorer baseline mean score of the PD-active group in the False Belief condition was consistent with the general findings in the literature.

The card sorting task reported in this study has, however, been used only twice previously in PD. Mengelberg and Siegert (2003) reported poorer performance of PD

participants in the False Belief condition, with a mean score that was almost identical to the current findings of the PD-active group at baseline. This mean performance score in PD was replicated by Nicolson (2016). Her study examined patients at baseline who participated in the current trial. The majority of Nicolson's PD patients (fifteen) were among the first randomized into the Enrichment trial and are included in the present analysis. This participant overlap allows consideration of what factors may have influenced the better performance of the PD-passive group at baseline, which was commensurate with that of the HC group.

It is possible that the improvement in performance of the PD-active group at end-of-trial was due to some benefits associated with the intervention. The PD-passive group showed only a mild, non-significant decline from baseline to end-of-trial. Based on the equivalent mean performance of the PD-passive group and PD-active groups at end-of trial, it is possible that the PD group examined in this ToM study may have been at an earlier stage of cognitive impairment than those tested by Mengelbert and Siegert (2003). Alternatively, the ToM deficit may be a specific deficit that is relevant only to a subset of non-dementing PD patients, and this deficit may be sensitive to non-pharmacological intervention.

The poorer baseline False Belief performance in the PD-active group was unrelated to deficits in more general cognition, because their mean scores in the other conditions, which controlled for sequencing deficits unrelated to ToM, was comparable to those in the HC group.

Mengelbert and Siegert (2003) also reported that PD participants with higher levels of depression performed more poorly on ToM tasks than PD participants with lower levels of depression. In the current study, however, the poorer ToM performance at baseline for the PD-active group versus the PD-passive group was unlikely to have been related to scores on depression or anxiety, as there were no significant correlations between these measures. Although the PD group as a whole had significantly higher baseline HADS anxiety and

depression scores than the HC group, there were no differences between the two PD groups for depression or anxiety. It also seems unlikely that the difference in findings derives from the use of different depression inventories (BDI versus HADS) as opposed to other methodological differences, especially the cognitive skills of participants in the two studies.

Other studies using alternative measures of cognitive ToM indicate that a selective impairment is present in at least moderate-stage PD, with preserved performance at earlier clinical stages (Kawamura & Koyama, 2007; Peron et al., 2009; Roca et al., 2010). Cognitive ToM is associated with the dorsolateral PFC and the central executive network. Therefore, if the Enrichment trial intervention has had any effect on cognitive ToM performance, it may be related more to activation of other brain networks than the DMN, which recruits medial portions of the PFC and is implicated in affective ToM. PD impairment in affective ToM typically emerges at later stages of the disease process (Poletti et al., 2012). As such, longitudinal follow up of the Enrichment trial cohort using an affective ToM task at a later stage, may shed light on whether there has been any long-term benefit of intervention on PD-vulnerable brain regions associated with the DMN. It will be important to follow the progress of both PD-active and PD-passive groups on this cognitive ToM card sorting task over time. If there has been an effect of intervention, the performance of the PD-passive group would be expected to fall compared to the PD-active group. This will help to establish whether an intervention effect has occurred at all, as based on this particular cognitive measure.

4.2 Autobiographical memory

Personal episodic and semantic ABM was measured with the Autobiographical Memory Interview (Kopelman et al., 1989). At end-of-trial, an adapted version of the Episodic Autobiographical Memory Interview (EAMI; Irish et al., 2008), was incorporated to facilitate a more fine-grained analysis of the contextual detail of episodic memories (Irish et al., 2008). This allowed scoring using both the AMI and EAMI. For the AMI, both personal semantic

memory and episodic memory was poorer in the PD participants than the HC groups. For semantic memory, based on the AMI, the PD-active group showed an intermediate level of recall between the HC group and PD-passive group, but there was no clear effect of intervention per se. On both the AMI and EAMI, all groups showed a drop in semantic memory for Recent Life at the end-of trial compared to Recent Life at baseline. This may have been due to the exclusion of the last 12 months for end-of-trial testing. For episodic recall using the AMI scoring method, both PD groups performed more poorly than the HC group and there was no effect of intervention. The more detailed autonoetic-based scoring afforded by the EAMI suggested that PD episodic memory at end-of-trial was poorer for more later adulthood and recent memory and that Childhood and Early Adulthood episodic memories were not impaired, compared with the HC group. However there was no significant interaction, and again, overall, results showed poorer recall in the PD groups versus the HC group and no effect of intervention.

4.2.1 AMI semantic memory

The impaired semantic recall in the PD group compared with HC group on the AMI, contrasts with a previous report examining personal semantic memory in PD. Smith et al. (2010) found that PDs showed relatively little difficulty in recalling autobiographical knowledge compared with events. Using the autobiographical fluency task, they reported no difference between PD and HC in recall frequency of names associated with each of five life periods. Smith et al. (2010) tested 16 PDs and 16 HC, whereas the current study compared 40 PD and 24 HC. Apart from procedural differences, it is possible that the earlier study was not powered to detect impaired semantic memory in PD. For the AMI, the current study found a temporal gradient with higher recall for Recent Life, which is a typical finding using the AMI (Piolino et al., 2002). This contrasts with the findings of Smith et al. (2010), who reported a lower frequency of names recalled in the last two time periods for both HC and PD groups. It

is possible though that using just one type of personal semantic knowledge (recall of names) may have biased results. These results also do not reflect the findings in the literature more generally, which is that semantic memory tends to stabilise and improve with age (Piolino et al., 2002).

It is unlikely that the time lag between assessment points contributed to the lower semantic scores for all groups at end-of-trial compared with baseline, again because semantic memory recall in normal ageing is relatively immune to age and retention effects (Irish et al., 2010). Rather, fatigue effects may have contributed to lower performances, as the end-of-trial assessment was three times the length of baseline (40 minutes: 2 hours). Fatigue is one of the more insidious symptoms of PD and tends to develop early in the disease process. It may have mediated the particularly low end-of-trial scores of the two PD groups for Recent Life compared with baseline, as this was the last section of the extended end-of-trial ABM interview.

It is possible that performance was also influenced by the exclusion of the twelve months leading up to test date for some questions, which was necessary to avoid the Enrichment trial and maintain 'blind' retesting conditions. As participants were unable to use places or names that applied to the last 12 months, questions that could have been answered easily at baseline may have been inapplicable at end-of-trial and resulted in low scores. For example, participants were asked to provide the names of neighbours from within the last six years but excluding the previous twelve months (S.4.4.5). For many, this would be difficult to answer unless they had neighbours who had moved out between one and five years ago

Therefore, this question could have been improved; however it was also a priority to keep amendments to the AMI as minimal as possible to retain continuity with the baseline schedule. Overall, five of 15 AMI questions (eight from 21 points) were affected by such

readjustments (S.4.4.1. - S.4.4.5.), and therefore the possible effect on scores cannot be discounted.

There were no significant differences in performance between the PD-active and PD-passive groups on the AMI semantic schedule. The PD-active group was, however, not significantly different to the HC group across the two trial points. Inferring any intervention effects in the slightly higher scores of the PD-active group at end-of-trial is compromised because of this group's higher scores at baseline also. The sample size in the two PD groups was relatively low, so an increased sample size would provide a better test of whether there is a beneficial effect of the Enrichment programme for Childhood and Early Adulthood events, suggested by Figure 3.10.

4.2.2 EAMI semantic memory

Performance on the EAMI semantic subscale between HC and PD groups for semantic memories differed for Later Adulthood only, especially Recent Life. This pattern of PD group impairment was similar to that of the aMCI group reported by Irish et al. (2010), in which EAMI semantic recall deficits began to emerge from the Middle Adulthood period onward (this period was not included for analysis in the current study due to time constraints on the length of testing). All groups showed a decline in EAMI semantic memory for recent life, and the more pronounced deficit at this epoch for the PD groups, may, again, have been influenced by fatigue during the final stages of the interview process. By comparison, the HC group performance for Recent Life was almost the same as for Childhood life period, as it was for the elderly control group used in the study by Irish et al. (2010). The similar semantic recall scores for Childhood life period for both HC and PD groups highlights the relative resistance of semantic recall to the effects of age compared with episodic memory. This finding also highlights the intactness of PD semantic recall for earlier years. Sub-analysis of the Childhood period shows comparable performance with HC across age periods. From

these results, it appears that decrements in semantic recall in PD emerge in Later Adulthood. However this may occur sooner, as it appears to in aMCI (Irish et al., 2010). Future work should look to explore semantic recall performance in Middle Adulthood.

Overall, the PD and HC groups showed similar performance gradients on the AMI and EAMI semantic schedules at end-of-trial. A major procedural difference between the two scales was the addition of Later Adulthood life period in the EAMI, which facilitated closer examination of semantic recall across the life span. These aspects of investigation are important because age related temporal gradients in PD personal ABM are not well-characterized in the literature. Unlike the EAMI, however, the AMI semantic memory scores showed differences between the groups across all life periods (Childhood, Young Adulthood, and Recent Life) when aggregating baseline and end-of-trial scores. Hence the EAMI and the AMI may produce a different pattern when comparing PD and HC groups. This might be explained by the AMI semantic schedule containing more specific, and date-based questions relating to particular themes (e.g. a wedding, children, hospitals and institutions) than the EAMI, which rotates names of people, activities of living and one important date across its life periods

4.2.3 AMI episodic memory

Findings on the AMI episodic schedule showed a robust difference in recall between the PD group and HC group across the three life periods, with less detail recalled by the PD group. Although personal ABM has not been widely researched in PD, the deficit in recall of detail, suggested by the lower scores of the PD group on this scale, are consistent with the findings of previous investigations (Nicolson, 2016; Sagar et al., 1988; Smith et al., 2010; Souchay & Smith, 2013); as well as studies which have examined episodic memory for public events and source memory (Gabrieli et al. (1996); Johnson et al. (2005); as cited by Souchay and Smith (2013)). Compared with baseline, end-of-trial AMI episodic scores were higher for Early

Adulthood, remained stable for Recent Life and got significantly worse for Childhood life period. Low recall for events from Childhood period at end-of-trial reduced further when analyses excluded memories not previously produced at baseline testing, suggesting fewer exemplars may be available during this period. However, overall these findings did not produce any clear evidence of a temporal gradient. The similar pattern of scores across life periods on the semantic and episodic schedules at end-of-trial, suggests a lack of discrimination between specific and more general, semanticised levels of event detail, which is a noted limitation of the AMI (Piolino et al., 2002). Absence of clear temporal effects is consistent with the findings of Sagar et al. (1988) using the cue-word task, but not Smith et al. (2010), who found evidence of greater impairment for more recent life periods on the autobiographical fluency task. There was, however, no discernible effect of intervention on episodic recall in this study, as PD-active and PD-passive groups showed no differences in scores at end-of-trial.

4.2.4 EAMI episodic memory

Performance on the EAMI episodic subscale also showed that the HC group recalled more contextual details for events than the PD group across all four life periods examined. For the HC group, memories for events became increasingly contextually detailed in more recent life periods, which is consistent with the gradient of recall in elderly controls reported by Irish et al. (2010). The same general pattern was evident in the PD participants. The suggestion of an improvement only for early adult life after intervention was not statistically supported; it may provide a target hypothesis for future study. More pronounced deficits have been reported for aMCI and, unsurprisingly, in AD (Irish et al., 2011a; Irish et al., 2010). An EAMI sub-analysis of the Childhood period showed that the superior episodic recall for the HC group was not evident for events prior to school, consistent with the indications in the literature that fewer memories are encoded before six years of age, with almost none encoded before the

age of three (Piolino et al., 2002). Clearly, however, PD can impede recall of events even during teenage years. This pattern of results suggests that even in early PD, when cognition is relatively intact using standardised neuropsychological tests, the disease has a negative impact on episodic memory across the lifespan, not just for recent periods since the onset of the illness. This was suggested by the preliminary findings of Nicolson (2016), and has been confirmed using measures that more directly capture the sense of autonoetic re-experiencing that is central to a truly episodic memory. To the author's knowledge, this is the first time these findings have been shown in the research literature.

Overall, results showed no major differences in performance between the PD-active and PD-passive participants at end-of-trial assessment on these semantic and episodic measures of ABM. This may be due to a lack of sufficient sample numbers and power, or that any effects of intervention on ABM performance may emerge over the long-term and at future follow-up assessments points. The other alternative is that there are no effects of the intervention, either now or in the future.

Long-term follow up will be critical considering the intervention itself was designed using the most current evidence to show benefits to cognition of physical and cognitive exercise in PD (Bloem et al., 2015; Hindle et al., 2015; Hindle et al., 2013). It is also possible that negative findings on the ABM measure was due to disguised intervention effects, resulting from uncontrollable factors such as generally more vigorous lifestyles within the PD-passive group than the PD-active group. Another consideration is that the heterogeneity of PD symptoms across individuals meant that patients within the PD-active arm may have benefited differentially from the intervention regimen (Bloem et al., 2015). It will be possible to explore these and other possible influencing factors further in the future, as the participants in this study were well-characterised due to regular and comprehensive collection of clinical, ecological and lifestyle data.

Chapter 5: Summary, limitations and concluding remarks

The aim of the current study was to examine performance on tasks measuring autobiographical memory and cognitive theory of mind in a cohort of well-characterized non-MCI PD patients, as part of a two-armed randomized controlled trial assessing the effects of a lifestyle intervention package on cognitive performance. Part of the novelty of this research was the inclusion of an adapted version of the Episodic Autobiographical Memory Interview (EAMI; Irish et al., 2010), which allowed analysis of contextual details associated with the experience of episodic recall. Both episodic autobiographical memory and theory of mind are associated with brain regions that form part of the default mode network, which shows evidence of reduced functional connectivity in cognitively unimpaired PD (Tessitore et al., 2012).

5.1 Key findings

The intervention was designed to target large scale brain networks that are vulnerable in PD including the default mode network, which was targeted with a subset of cognitive exercises and memory elaboration sessions.

Our findings showed that memory for personal facts and events was poorer in the PD participant group compared with HC. Of particular interest was that PD participants showed impairment in the recall of contextual details associated with the autonoetic experience of episodic recall, which suggests that even in early PD, episodic memory is affected across the lifespan and prior to the onset of the illness. Contrary to our expectations, we did not find any clear evidence of an effect of the intervention in measures of ABM, as there were no differences in performance between the active and passive PD groups. This is most likely to have been due to the low power of the study.

For cognitive Theory of Mind, our findings showed the PD-active group performed more poorly at baseline than the PD-passive and HC group, but matched their performance at

end-of-trial assessment. As cognitive ToM is more closely associated with other large-scale brain networks than the default mode network, it is possible that elements of the intervention targeting such networks may have conferred some beneficial effect on performance.

5.2 Limitations

Study limitations related predominantly to the ABM aspect of this study rather than to the examination of ToM. One concerned the 'blinded' end-of-trial testing conditions between the PD and HC group. One assessor tested the PD participants, and another tested the HC group, which raises the possibility that the data may have been vulnerable to interrater variability. Notwithstanding, the AMI and EAMI semantic interview schedule questions were scripted to reduce this risk. Similarly, the structured format of the EAMI involved a systematic, checklist-style approach which testers were encouraged not to deviate from.

The difference in the length of interviews between baseline and end-of-trial may have had a fatigue effect that affected results, although participants were offered refreshments throughout. Findings may also have been influenced by the small variations made to the format of the AMI for follow-up testing.

The difference in episodic scoring methodology between PD and HC groups may have influenced the findings. Event interviews with all PD participants were transcribed and scored off paper. However due to time constraints, events for the HC group were scored from audio. Efforts were made to ensure consistency of scoring, including scoring HC events only after completion of the PD groups to ensure proficiency was accurate and efficient. Also, regular checks for consistency were made. PD event material was re-scored regularly from audio and compared with scores based off transcribed material.

Despite these limitations, to the best of our knowledge this study is the first within the framework of PD to examine details of event recall closely associated with autonoesis and

episodic memory and find impairment; and also find impairment in recall for personal semantic memory.

5.3 Future Directions

This combined physical and cognitive enrichment intervention package was designed using the most current evidence that show benefits to cognition of physical and cognitive exercise in PD (Hindle et al., 2013). Although the sample size was relatively small, findings suggest that a relatively intensive combination of cognitive and physical exercises does not benefit PD participants prior to an MCI status. However, further follow up is required to test whether intervention effects emerge over the longer term.

For ABM, future directions include further assessment of aspects of the semantic and episodic memory assessments; and for ToM, follow-up will concern investigating the progress of both PD-active and PD-passive groups on this card sorting task over time. Introduction of an affective theory of mind task would also provide an additional measure of the DMN alongside the measures of personal ABM. This is of particular importance in PD, on the basis of fMRI evidence which indicates reduced functional integrity of the default mode network even in patients with relatively normal cognition.

Long-term follow up is critical considering the intervention itself was designed using the most current evidence to show benefits to cognition of physical and cognitive exercise in PD (Bloem et al., 2015; Hindle et al., 2015; Hindle et al., 2013). In future studies with larger sample sizes, subgrouping and clustering of PD patients based on cognitive and motor symptom profiles may also be beneficial to examining whether subgroups benefit differentially from different intervention regimens.

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Appendix A: Theory of Mind card sorting task

Scripted instructions

Place the pile of cars in front of you facing the participant.

“In front of me I have a pile of cards. A set is made of four cards. On the back of each card is a number. The number does not mean anything. I simply use the numbers to pre-arrange a mixed-up order of stories for each person to see. There are also coloured dots. I simply use these to record the order of cards when you’ve arranged them. I am going to put these four cards face-down in front of you.”

Place the cards in the pre-arranged order on the table face-down.

“When we are ready to start, I will ask you to turn the cards over. You can do that in any order that you like, that’s entirely up to you. Once you have turned the cards over, your task is to line the cards up in a straight line, like a comic-strip, first card here, second card here, etc.”

Point to where you want the cards lined up on the table.

“You need to arrange the cards in the correct order so that they show a logical sequence of events. When you are happy that you have the cards in the correct order, or that you have done your best to work out an order that makes the most sense, I want you to say ‘finished’. I will be using this stopwatch to record how long you take from the time that I say turn the cards over ‘now’ to the time that you say ‘finished’. Having said that, I don’t want you to worry about being timed. It is more important to get the cards in the correct order than it is to be fast. Let’s try the first story. This is a practice so that you can get used to doing the task. When I say ‘now’, I want you to turn the cards over. Ready, turn the cards over now”.

Start the stopwatch on ‘now’, and proceed to give the participant feedback as to whether they were correct or not. Also use this teddy-bear picture sequence to point out to subjects that

these are not the sort of picture sequences where every detail of the story is shown on every card.

“Notice that in this sequence you can’t tell that the boy wants the teddy-bear until the last card. In all of the sequences that you will do the cards are like that. You will need to make some inferences to work out how best to put the cards together. Now we’ll do a second practice” and proceed as above.

“Now we’ll move on to the other stories. There are 16 stories in total. You may find that some of these stories are less straightforward than others. If you find a set of cards confusing, just do your best to put the cards in an order which you think is the most sensible. You will see the 16 stories in a mixed-up order. That means that the stories will not start out easy and get progressively harder. You might do one story that seems a bit confusing and then the very next story could be very easy. Just work through each story at your own pace. Do you have any questions? OK, let’s start with this story”.

Lay the first story out in the predetermined order (L-R for participant. R-L from examiner’s view). Say, *“**You can turn the cards over now”***. Begin timing. Stop timing when the participant indicates they are finished and record the order of the cards on the score sheet and the time taken. Pickup from R-L from examiner’s view and fan downwards. Record any errors before allowing the participant to fix them.

Appendix B: Cognitive Theory of Mind assessment scoring sheet

Picture Sequencing Task

Sub ID: _____

Story	Layout order	Time taken	Subject order (colour id → no. id)	Correct order	Score	Story
Prac 1						Prac 1
Prac 2						Prac 2
3	OGYB			BYGO		3
9	YGBO			BYGO		9
17	OBYG			GYOB		17
12	GYOB			GYBO		12
18	YBOG			BGOY		18
10	YOBG			GYBO		10
5	YGBO			YOBG		5
14	OYBG			YBOG		14
8	YBOG			GBYO		8
15	BGYO			YOGB		15
7	GOYB			OBYG		7
11	BGYO			YBGO		11
4	BGOY			OBYG		4
13	GBOY			OBYG or OBGY		13
16	GYOB			BOYG		16
6	GYBO			OYGB		6

Appendix C: Examples of the four DMN cognitive tasks

Examples of the four cognitive tasks from the Enrichment Trial designed to stimulate the Default Mode Network: Moral Dilemmas; Reading the Mind in the Eyes; Envisioning the Future; Faux Pas Story.

C.1. Moral dilemmas task

Moral Dilemmas - STORY 1

Read the story and then CIRCLE the answer YOU would most likely give, first for the "Moral Decision" and then for the "Non-Moral Decision".

Mr. Jones is fishing and sees some tourists sailing for a nearby island. Soon after, Mr. Jones hears that there is a violent storm coming that will hit the tourist's boat. The only way he can warn them is by stealing a speedboat which belongs to a spiteful old man. If Mr. Jones does not steal the boat the storm will sink the tourists' boat. If he steals it, the boat owner will bring charges against him.

Moral Decision – If you were Mr. Jones, what would you do?

Choose either STEAL THE BOAT or NOT STEAL THE BOAT

Non-Moral Decision – If you were the tourists how would you be feeling?

Choose either EXCITED or UNHAPPY

C.2. Reading the mind in the eyes task

Choose and circle which word best describes what the person in the picture is thinking or feeling.

Panicked Flustered Angry

C.3. Envisioning the future task

Envisioning the Future – Task Sheet (5-2)

Trekking to the South Pole

You and your friends have decided to go on a trek to the South Pole. You plan to go mid-summer so will have just over 6 months to prepare and train. This will be a tough trip taking 60 days and over a distance of 1000kms.

Your task: Give a description of what you will need to do prepare for your trek.

It is important that you imagine and then visualise in your mind to help expand your description.

.

C.4. Faux pas story task

Story 1. Kim's cousin, Scott, was coming to visit and Kim made an apple pie especially for him.After dinner, she said, "I made a pie just for you. It's in the kitchen.""Mmmm," replied Scott, "It smells great! I love pies, except for apple, of course."

1. 1.Did anyone say something they shouldn't have said or something awkward? **If yes**, continue with all questions. **If no**, skip to question 7.
2. Who said something they shouldn't have said or something awkward?
3. Why shouldn't he/she have said it or why was it awkward?
4. Why do you think he/she said it?
5. When he smelled the pie, did Scott know it was an apple pie?
6. How do you think Kim felt?
7. In the story, what kind of pie did Kim make?
8. How did Kim and Scott know each other.

Appendix D: Elaboration session sketches of participant homes from childhood and early adulthood

Participants' sketches of their homes from childhood and early adulthood, drawn during the course of memory elaboration sessions.

Appendix E: Example memories provided at baseline

Three AMI events provided at baseline by one participant who was later randomized into the PD-Enrichment Intervention trial arm. These memories were used for memory elaboration sessions. Reproduced with permission. All names have been changed.

E.1. Event 1.3. An event from high school

There were many (events). James Cowan and I used to play golf pretty much every night of the week, the school had an 18 hole golf course at that time and, because we had a shortage of golf balls, he was a big solid guy, and he would walk ahead of me to stand on the golf balls so that no one could find the most of the other guys walked past and I'll go around and pick them out of the ground. So we collected our own golf balls!

When was this?

Oh, in our more senior high school years.

So he was that big guy?

Yeah, bigger guy the balls were on the ground and when we were short of balls he would stand on them with his weight and very has ball on the ground. Pays to pick them out of the ground after everyone went past.

Because nobody could see it!

We had some interesting times. And we're still friends to this day.

Did you continue to play golf for years after high school?

No, we would like to go back and try playing it again, we haven't had time. In years I haven't had time.

So whereabouts was that?

We had an 18 hole golf course around the school. It started at Magee block and ended up around the southern dormitory area, at the back of Centennial Park.

E.2. Event 2.1. An event from a wedding

Yes I had my arm in a plaster. Because I had just had an operation to get my hand rebuilt which I had got damaged in Australia when I was working there. So I had to attend a wedding as a best man with arm in a sling. Yes, that was were remembered. Yes the bridesmaids name was (*name).*

Do you remember any particular moment, or anything that stands out to you?

We had to drink a wine to the bride, a "Here's to the bride". And I couldn't drink with my left hand and I spilt all over the place! From then I did no more "Here's…" to anybody!

And where was the toast held? Where was the reception held?

It was held at those rooms down the middle of town on the left-hand side, by Taggerty's where that shop used to be. Something or other rooms. I can't remember the actual name of the rooms but I know their physical location. In the middle of Oamaru, past the statue, second on the left. There is a pub restaurant at the front of it and the rooms are in the back behind it. The name of the hotel thing. It's entertainment rooms especially for weddings, at the back of the hotel. A side alley entrance and everything.

You know it!

I definitely know it!

E.3. Event 4.3. An event related to a holiday or journey

Can you recall a particular event or incident that took place on any holiday or journey within the last five years?

Yes, I was sitting in an outside restaurant in Akaroa having a nice cup of coffee, and a bird came along and shat on my head. They tell me it was supposed to be good luck but ever since then I've had bad luck.

Oh no! Which restaurant was that?

(silence)

Yes, there is a danger with those restaurants out on the promenade and agora because there shouted baked tall canopies of trees which are just like long drops for the birds aren't they!

Oh, yes, well and truly!

Isn't that funny. So, you were sitting outside, did you say that you are enjoying a beverage?

Enjoying a nice cup of coffee. This buddy bird came along and shat clean on top of my head it didn't just kiss me, it gave me the whole lot.

Oh gosh. Do you remember which restaurant it was?

The one as you go around the bend towards, to where the war first, where the key is, where the higher the dolphin boats. It was just at the end of that key. Faces northwards. Because as you get down the bottom of the town the foreshore goes round the bend and turns right and gin you can then carry on that wake or carry on down through to down the pier.

So it was near the pier?

Just off the end of the pier.

That's hilarious!

Yes, you've got to have a chuckle don't you.

It might be good for your hair as well!

Laughter.

A bit of organic matter!

How long ago did this happen?

Oh, it must have been about 18 months ago or so.

Appendix F: Example of a memory elaboration session

Two transcribed excerpts of dialogue from memory elaboration sessions.

F.1. Example one

So we now just gonna think back to your time at high school and a particular incident that happened at that time. You mentioned earlier that there was an explosion in the lab following an attempt to generate hydrogen. Can you tell me more about this experiment?

We um, I think there were three of us in the science class. This was at Temuka district high school. And we needed some hydrogen for some experiment. And we had no way of getting it so I suddenly remembered that we used to have and experiment which the science teacher did alone, where you put a piece of sodium on some water and it bussed around and gave off hydrogen.

Okay.

So I said well, if we go off and get some sodium we can do this. Which we did. And we were holding a glass of what you call it a glass canister of some sort, And as the sodium ran round and round we were trying to track it with the glass thing to get the hydrogen in there. Because it gave off hydrogen.

Okay.

And that the thing fizzed out so we needed a bigger piece so we got quite a big piece and put it on… it must have been about 3cm square I suppose.

What colour was it?

Umm, it had a sort of orangey colour if I remember rightly. So round and round it went and we had this jolly thing we had to put the glass jar fairly close to get the hydrogen coming off. And suddenly there was a bang, And the whole thing blew up! Fortunately I was wearing glasses because you know, I would have got it in the face. Because we were all crouched over the jolly thing trying to do this. So yes there was water all over the floor and it really

could have been quite dangerous. So then we had to go and confess tp the science master who was taking a class somewhere else, what had happened! And he said when I left you you were doing some perfectly harmless experiment it was fine. And as soon as I turn my back you were… you do this. I think he was relieved that we were all safe because it could have been quite dangerous.

It could have been quite bad. Yeah.

But, so he didn't reprimand us or anything he just knew we'd failed and we'd made a mess we shouldn't have done it.

That you'd learned your lesson hopefully!

Apparently that experiment, we didn't know, but it had been banned from school.

Okay.

And we found that out after.

Because of how dangerous it was.

So we hadn't got to collecting hydrogen to do the other experiment!

But you certainly created it!

Oh yes we created some.

Mm. Can you describe for me again the glass and how you had the sodium in the water?

We had a basin of water.

Okay, a basin? Where was the basin located?

It was sitting on the bench probably.

Okay. So just like a pan of sorts?

Yeah. Like that.

Okay

F.2. Example two

Your reception was held in, south east border of London?

The wedding took place on the south east border of London in Penge Parish Church but then we went over the border to where by the time my wife was staying with relations and that was in Kent.

Okay and so how did you go over the border from south east London over to...?

By car. It was only 5 minutes away by car, to her relations.

Do you recall the trip, what the car looked like?

No I don't but I remember what happened just before it, nobody told me that we had choir boys because we had a small congregation at our wedding. And so we had choir boys helping us with the singing and church. Nobody told me however that you throw a heap of sixpences in the air for the choir boys to have a coin scramble.

Oh right.

I presume they got paid for being there because we got charged a certain amount for having a choir, so we presumed therefore that the choir boys got paid. Now I didn't know, it's a custom in England, that if you have choir boys you have a coin scramble afterward. And all these hopeful boys were sitting there standing around wondering when the coins were going to come! And they didn't come! Yeah so they were disappointed.

So that was inside the church still?

Just at the gate of the church entrance, on the street.

And you saw them standing there?

Yeah! I thought it was very good of them to stand and be there for us, as it were! I thought they would have packed up and gone home! But afterwards somebody told me what should have been done. I presumed that they thought that I knew about it anyway. But I was from down under I didn't know anything about that, nothing like that happened in New Zealand. They didn't usually have choir boys at a wedding!

Its easy to run into trouble with custom!

Yes well there was nothing I could have done about it. I think now I suppose I could have sent them some money and told them to distribute it among the choir boys.

So the choir boys, what did they wear?

They wore robes, and from memory they were up in a gallery by the organ pipes.

Appendix G: AMI and EAMI semantic memory item schedule

Organisation of questions for AMI and EAMI semantic items schedule, showing overlap between item questions.

	Childhood (age 0 - 18)			Early Adulthood (age 18 - early tthirties)			Later Adulthood (age 45 - 6 years ago)	Recent Life (within last 6 years - 12 months ago)
AMI Semantic Schedule	**Part 1 (max 5 points)**	**Part 2 (max 8 points)**	**Part 3 (max 8 points)**	**Part 4 (max 8 points)**	**Part 5 (max 9 points)**	**Part 6 (max 4 points)**		**Part 7 (max 8 points)**
	AMI 1.1. = S.1.1.1. (2)	AMI 2.1. = S.1.2.1. (1)	AMI 3.1. = S.1.3.1. (1)	AMI 4.1. = S.2.1.1. (1)	AMI 5.1. = S.2.2.1. & S.2.2.2. (2)	AMI 6.1. = S.2.3.1. (1)	~	AMI 7.1. = S.4.1.1. (1)
	AMI 1.2. = S.1.1.2. (3)	AMI 2.2. = S.1.2.2. (1)	AMI 3.2. = S.1.3.2. (1)	AMI 4.2. = S.2.1.2. (2)	AMI 5.2. = S.2.2.3. (2)	AMI 6.2. = S.2.3.2. (0.5)	~	AMI 7.2. = S.4.1.2. (1)
		AMI 2.3. = S.1.2.3. (1)	AMI 3.3. = S.1.3.3. (0.5)	AMI 4.3. = S.2.1.6. (2)	AMI 5.3. = S.2.2.4. (2)	AMI 6.3. = S.2.3.3. (0.5)	~	AMI 7.3. = S.4.1.3. (1)
		AMI 2.4. = S.1.2.4. (2)	AMI 3.3. = S.1.3.3.1. (0.5)	AMI 4.4. = S.2.1.4. (3)	AMI 5.4. = S.2.2.5. (1)	AMI 6.4. = S.2.3.4. (1)	~	AMI 7.4. = S.4.1.4. (2)
		AMI 2.5 = S.1.2.6. (3)	AMI 3.4. = S.1.3.5. (2)		AMI 5.5. = S.2.2.6. (1)	AMI 6.5. = S.2.3.5. (0.5)	~	AMI 7.5. = S.4.1.5. (3)
			AMI 3.5. = S.1.3.7. (3)		AMI 5.6. = S.2.2.7. (1)	AMI 6.6 = S.2.3.6. (0.5)	~	
							~	**Part 8 (max 8 points)**
							~	AMI 8.1. = S.4.4.1. (1)
							~	AMI 8.2. = S.4.4.2. (1)
							~	AMI 8.3. = S.4.4.3. (1)
								AMI 8.4. = S.4.4.4. (2)
							~	AMI 8.5. = S.4.4.5. (3)
								Part 9 (max 2 points)
							~	AMI 9.1. = S.4.3.1. (1)
							~	AMI 9.2. = S.4.3.2. (1)
								Part 10 (max 3 points)
							~	AMI 10.1. = S.4.2.1. (1)
							~	AMI 10.2. = S.4.2.2. (1)
								AMI 10.3. = S.4.2.3. (1)
EAMI Semantic Subscale	**(max 10 points)**	**(max 10 points)**	**(max 14 points)**	**(max 14 points)**			**(max 14 points)**	**(max 14 points)**
Daily Living								
Name of Association	S.1.1.4. (1)	S.1.2.1. (1)	S.1.3.1. (1)	S.2.1.2.2. (1)	~	~	S.3.4. (1)	S.4.4.7. (1)
Location	S.1.1.6. (1)	S.1.2.2. (1)	S.1.3.2. (1)	S.2.1.3. (1)	~	~	S.3.5. (1)	S.4.4.8. (1)
Nature of work/study/hobby	S.1.1.5. (1)	S.1.2.8. (1)	S.1.3.3. (.5) + S.1.3.3.1. (.5)	S.2.1.2.1 (1)	~	~	S.3.6. (1)	S.4.4.9. (1)
How travelled there	S.1.1.7. (1)	S.1.2.5. (1)	S.1.3.6. (1)	S.2.1.7. (1)	~	~	S.3.7. (1)	S.4.4.10. (1)
Names of People								
Full name	S.1.1.2. (1)	S.1.2.6. (1)	S.1.3.7. (1)	S.2.1.4. (1)	~	~	S.3.2. (1)	S.4.4.5. (1)
Full name	S.1.1.2. (1)	S.1.2.6. (1)	S.1.3.7. (1)	S.2.1.4. (1)	~	~	S.3.2. (1)	S.4.4.5. (1)
Full name	S.1.1.2. (1)	S.1.2.6. (1)	S.1.3.7. (1)	S.2.1.4. (1)	~	~	S.3.2. (1)	S.4.4.5. (1)
Relationship	S.1.1.3. (1)	S.1.2.7. (1)	S.1.3.8.(1)	S.2.1.5. (1)	~	~	S.3.3. (1)	S.4.4.6. (1)
Relationship	S.1.1.3. (1)	S.1.2.7. (1)	S.1.3.8.(1)	S.2.1.5. (1)	~	~	S.3.3. (1)	S.4.4.6. (1)
Relationship	S.1.1.3. (1)	S.1.2.7. (1)	S.1.3.8.(1)	S.2.1.5. (1)	~	~	S.3.3. (1)	S.4.4.6. (1)
Important Event Date								
Date	~	~	S.1.4.1. (1)	~	~	S.2.4.1. (1)	S.3.8. (1)	S.4.4.11. (1)
Month	~	~	S.1.4.1. (1)	~	~	S.2.4.1. (1)	S.3.8. (1)	S.4.4.11. (1)
Year	~	~	S.1.4.1. (1)	~	~	S.2.4.1. (1)	S.3.8. (1)	S.4.4.11. (1)
Location	~	~	S.1.4.2. (1)	~	~	S.2.4.1. (1)	S.3.9. (1)	S.4.4.12. (1)

Appendix H: End-of-Trial testing schedule

NZBRI Enrichment Study 2016-2017

Autobiographical Memory Retesting Schedule

ID
Date of Test
Age
Date of Birth

We are going to ask you questions about your life. These will cover your school days and adult life, including recent times.
This is something that has never been examined before: to see what details people with Parkinson's recall from their life, and to see whether these are similar to those without Parkinson's. To do this, we need to ask a lot of questions, so we will go through them at a fairly quick pace. It is perfectly normal for all of us to find these questions a little difficult. Asking about early life is especially difficult, no matter what someone's age. Just do your best and that will be fine.
Also, please do not divulge to me the participant group into which you were subsequently allocated for this study. I should not know anything about your activities during the time since you were previously tested.

Do you mind if I voice record this interview so that I can listen to it later on? Yes / No

---

Episodic Recall Sections

1. Participant engages in free recall of event.
2. Probe for further details using Event Recall Checklist
3. Investigate subjective recollective experience using Autonoetic Subscale, using Response Cards (R.C.)

Resources

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Piolino, P., Desgranges, B., Benali, K., & Eustache, F. (2002). Episodic and semantic remote autobiographical memory in ageing. *Memory (Hove, England)*, *10*(4), 239–257. http://doi.org/10.1080/09658210143000353

S.1. Childhood (0-18)

S.1.1 Period before school (0 - 5yrs)

S.1.1.1. Can you give me as much as possible of any home address before you went to primary school?

Full address = 2
Street *and* town only = 1
Town *or* street only = ½

S.1.1.2. Can you give me the first names and surnames of THREE friends, neighbours or acquaintances from the time before you went to primary school? If possible, try to restrict your answers to people only known during this period.

Each correct full name = 1
Each first name *or* surname only = ½

1.
2.
3.

S.1.1.3. For each person, what was their specific relationship to you? *(if not already provided and noted)*
(*Prompts:* For example, a neighbour or friend?)

Each correct = 1

1.
2.
3.

S.1.1.4. Can you remember any regular activity or outing you took part in before you started primary school, outside home?

Correct = 1

S.1.1.5. Who did you go with usually, on that outing?

Correct = 1

S.1.1.6. Can you give me the name or location of the place you went?

Correct = 1

S.1.1.7. How did you travel to this place? (*Prompts:* For example, driving or by bus?)

Correct = 1

E.1.1. I would now like you to describe out loud, **and with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* from the period **before you went to school**. *Prompts:* 'Your first memory?', 'Involving your family, such as a brother or sister?', "A trip somewhere?', "A church event?")

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

S.1.2 First school (5 - 11yrs)

S.1.2.1. Can you give me the name of your primary school? (*main*)

Correct = 1

S.1.2.2. Can you give me the location of this primary school?

Town or city = 1

S.1.2.3. What was your age when you started at this school?

Correct = 1

S.1.2.4. What was your home address when you started at this school?

Full address = 2
Street *and* town only = 1
Town *or* street only = ½

S.1.2.5. How did you mainly travel to and from this primary school? (*Prompts:* For example, in a car, by bus?)

Correct = 1

S.1.2.6. Can you give me the first names and surnames of THREE teachers and friends from this school?
Try not to use names you gave earlier.
(*Prompts:* 'The head teacher?', 'Your form teacher?', 'A friend?')

Each correct name = 1
Each first name *or* surname only = ½

1.
2.
3.

S.1.2.7. For each person, what was their specific relationship to you? *(if not already provided and noted)*

Each correct = 1

1.
2.
3.

S.1.2.8. Name one regular activity you took part in at this primary school.

Correct = 1

E.1.2. I would like you to describe out loud, and **with as much detail as possible,** an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred **while at primary school** (age 5-11 years). (*Prompts*: 'Involving a teacher?', 'Involving a friend?' 'A church event, such as your first communion?')

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how you felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

S.1.3 Main secondary or high school (11 - 18yrs)

S.1.3.1. Can you give me the name of your main high school?

Correct = 1

S.1.3.2. Can you give me the location of this high school?

Town or city = 1

S.1.3.3. What was the highest qualification level you obtained at high school?

Correct level = ½

S.1.3.3.1 How many subjects did you take at this level?

Correct number = ½

S.1.3.4. What year did you leave or graduate from high school?

Correct year = 1

S.1.3.5. Can you give me as much as possible of any home address when you were attending high school?

Full address = 2
Street *and* town only = 1
Town *or* street only = ½

S.1.3.6. How did you mainly travel to and from this high school?

Correct = 1

S.1.3.7. Can you give me the names and surnames of THREE teachers and friends from your main high school?
Please try not to use names already provided.
(*Prompts:* 'The head teacher?', 'Your form teacher?', 'A friend?'

Each correct name = 1
Each first name *or* surname only = ½

1.
2.
3.

S.1.3.8. For each, what was their specific relationship to you? *(if not already provided and noted)*

Each correct = 1

1.
2.
3.

S1.4.1. I would like you to try to remember an important event that happened at any time up to when you were 18, such as a birth, a party, a family event, or death.

Can you give me the complete date of this event, as much you can remember?

Date + month + year = 3

Date	-
Month	-
Year	-

S.1.4.2. Can you give me the location of this event?

Town or city = 1

E.1.3. I would like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred while **at high school** (age 11-18 years). (*Prompts:* 'Involving a teacher?', 'Involving a friend?', 'Your confirmation?)

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

S.2. Early Adult Life (18-30)

S.2.1 Career

S.2.1.1. What qualifications did you obtain after leaving school?

Correct recall or stating 'no qualifications' = 1
'Don't know' = 0

S.2.1.2. ***(IF** qualification(s) obtained):* What was the name of your course and educational institution?

Name of course = 1
Name of institution = 1

Course	-
Institution	-

What was your first job after completing your education?

Correct = 1

and name of firm or organization

Correct = 1

S.2.1.3. Can you give me the location of your first job?

Town or city = 1

S.2.1.4. Can you give me the first names and surnames of THREE friends, teachers or colleagues from this period?
Try not to use names you have already given.
(*Prompts:* 'The Principal' *or* 'The boss?', 'The tutor' *or* 'Your foreman?', 'Any classmates' *or* 'Any workmates?')

Each correct name = 1
Each first name only = ½

1.
2.
3.

S.2.1.5. For each person, what was their specific relationship to you? *(if not already provided and noted)*

Each correct = 1

1.
2.
3.

S.2.1.6. What was your address while in your first job?

Correct = 2
Street and town only =
Town or street only = ½

S.2.1.7. How did you mainly travel to and from your first job?

Correct = 1

S.2.2. Wedding

S.2.2.1. (***IF*** *married between late teens and early thirties):* What date were you married?

Correct = 1
Year only = ½

S.2.2.2. *and* the place where you were married?

Town or city = 1

(OR *if not married in this time period):* Can you give me the name of someone else whose marriage you attended between 18 and your early thirties?

Correct = 1

and the place where this marriage was held?

Town or city = 1

S.2.2.3. What was your home address <u>before</u> this wedding?

Correct = 2
Street and town only = 1
Town or street only = ½

S.2.2.4. What was your address immediately after this wedding?

Correct = 2
Street and town only = 1
Town or street only = ½

S.2.2.5. What was the name of the best-man from this wedding (or any guest)?

Correct name = 1
First name only = ½

S.2.2.6. What was the name of the bridesmaid from this wedding (or a guest)?

Correct name = 1
First name only = ½

S.2.2.7. What was the bride's (or your own) maiden name (or a guest)?

Correct name = 1
First name only = ½

S.2.3. Children

S.2.3.1. What is the name of your first child (or nephew / niece / child of a close friend)?

Correct = 1

S.2.3.2. What is the date of birth of this child (or age of a nephew, niece or child of a close friend)?

Correct year = ½

S.2.3.3. Where was this child born?

Town or city = ½

S.2.3.4. What is the name of your second child (or nephew / niece / child of a close friend)?

Correct = 1

S.2.3.5. What is the date of birth of this child (or age of a nephew, niece or child of a close friend)?

Correct year = ½

S.2.3.6. Where was this child born?

Town or city = ½

S.2.4.1. I would like you to try to remember an important event that happened at any time from when you were 18 to your early thirties. This could be a ceremony or celebration, or a birth or a death that you have not already given as an answer.

Can you give me the complete date of this event, as much you can remember?

Date + month + year = 3

Date -
Month -
Year -

S.1.4.2. Can you give me the location of this event?

Town or city = 1

E.2.1. I would now like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred **between the ages 18 and 30.** For this memory, I would like you to recall an event from a **wedding, or another type of family occasion**. (*Prompts:* 'A family holiday?', 'The day of a birth?')

Description / Free Recall:				
		Prompts	**Notes**	**Score**
	1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
	2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
	3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
	4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
	5. Emotion	Can you recall how <u>you</u> felt at the time?		
	6. Thoughts	Can you remember what you were thinking, at the time?		
	7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
			Total Score	

E.2.2. I would now like you to describe out loud, and **with as much detail as possible**, another incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between the ages 18 and 30. For this memory, I would like you to recall an event or meeting related to a **specific person**.
(*Prompts:* 'A first encounter with someone (the day you met somebody new)?', 'A first meeting with your spouse?', 'A day with a friend?')

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

E.2.3. I would now like you to describe out loud, and **with as much detail as possible**, another incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between the ages 18 and 30. This time, I would like you to recall an event from your **college* or professional life**. (*Prompts:* 'Your first day at work or college?', 'An incident with a friend?', 'A day with a teacher?') *(*Only if still studying after 18, and incl. apprenticeships)*

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how you felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

S.3. Late Adulthood (45yrs to 6 years ago)

S.3.1. Can you give me as much as possible of any home address after you were aged 45 up to **about 6 years ago**, that is *not also your current address*? (if possible)

Correct = 2
Street and town only = 1
Town or street only = ½

S.3.2. Can you give the names of THREE people from among your friends or acquaintances during this period?
Try not to use names you have already given.
Prompts: "The name of a friend, a neighbour, a doctor, a teacher or a colleague?"

Each correct name = 1
Each first name only = ½

1.
2.
3.

S.3.3. For each, what was their particular relationship to you? *(if not already provided and noted)*

Each correct = 1

1.
2.
3.

S.3.4. Can you give me the name of an institution or association you were involved with between ages 45 and up to six years ago, related to your work, study or a hobby?

Correct = 1

S.3.5. Where was this place located?

Town or city = 1

S.3.6. What kind of hobby / study / work was this?

Correct = 1

S.3.7. How did you typically travel to this place from home?

Correct = 1

S.3.8. I would like you to try to remember an important event that happened at any time during this time period.
This could a ceremony or celebration, or a birth or a death.

Can you give me the complete date of this event, or as much you can remember?

Date + month + year = 3

Date	-
Month	-
Year	-

S.3.9. Can you give me the location of this event?

Town or city = 1

E.3.1. I would now like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between when you were aged **45 until 6 years ago**. I would like it to be related to a **trip or a journey**. (*Prompts*: 'At the place you visited?', 'Involving someone you met?', 'While you were travelling?')

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

E.3.2. I would now like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between when you were aged 45 until 6 years ago. This time, I would like your memory to be related to a **family event or occasion**. (*Prompts:* 'A birthday?' 'Christmas day?', 'A death?)

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how you felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

E.3.3. I would now like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between when you were aged 45 until 6 years ago. I would like this event to be related to your **professional life or retirement.**
(*Prompts:* 'Something unusual that happened at work?', 'A day with your grandchildren?', 'A day you went somewhere special?')

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

S.4. Recent life, within the last 6 years

S.4.1. Present or recent hospital or institution

S.4.1.1. Can you give me the name of a hospital or medical place you have attended recently (or in the last 12 months)?

Correct = 1

S.4.1.2. Can you give me the location of this place?

Town or city = 1

S.4.1.3. What date did you arrive at this hospital or institution?

Month or year = 1

S.4.1.4. Can you give me as much as possible of your current home address?

Correct = 2
Street and town only = 1
Town or street only = ½

S.4.1.5. Can you please try to remember the names of THREE staff members or fellow patients connected with this medical place? (Or the names of three current neighbours or colleagues)

Each correct name = 1
Each first name only = ½

1.
2.
3.

S.4.2. Holiday or Journey

S.4.2.1. Can you give me the name of a place you have visited on a holiday or journey in the last year (or within the last six years)?

Correct = 1

S.4.2.2. In which month (or year) did this holiday/journey take place?

Month or year = 1

S.4.2.3. Can you give me the name of a person with whom you went on this holiday/journey?

Correct name = 1
First name only = ½

S.4.3. Last Christmas

S.4.3.1. Can you give me the name of the place where you spent last Christmas?

Correct = 1

S.4.3.2. Can you give me the name of a person with whom you spent last Christmas?

Correct name = 1
First name only = 1/2

S.4.4. Previous hospital or institution and activities between 6 years – 12 months ago

S.4.4.1. Can you give me the name of a previous hospital or medical place you visited, from within the last 6 years but excluding the last 12 months?

Correct = 1

S.4.4.2. What was the location of this place?

Town or city = 1

S.4.4.3. What date did you visit or arrive at this place?

Month or year = 1

S.4.4.4. What was your home address when attending this place?

Correct = 2
Street and town only = 1
Town or street only = ½

S.4.4.5. Can you give me the names of THREE friends, colleagues or acquaintances connected with your visits to this medical place?
(Or the names of three neighbours from between 12 months and 6 years ago)

Each first name only = ½
Each correct name = 1
Each first name only = ½

1.
2.
3.

S.4.4.6. For each, what was their relationship to you? *(if not already provided and noted)*

Each correct = 1

1.
2.
3.

S.4.4.7. Can you give me the name of an institution or association you were involved with between the last <u>six years up to twelve months ago</u>, related to a hobby, study or work?

Correct = 1

S.4.4.8. Where was this place located?

Town or city = 1

S.4.4.9. What kind of hobby / study / work was this?

Correct = 1

S.4.4.10. How did you typically travel to this place?

Correct = 1

S.4.1. I would like you to try to remember an important event that has happened at any time from within the **last six years up to twelve months ago.**
This could be a birth, a death or a ceremony or celebration.

Can you give me the complete date of this event, as much you can remember?

Date + month + year = 3

Date	-
Month	-
Year	-

S.4.4.12.Can you give me the location of this event?

Town or city = 1

E.4.1. I would now like you to describe out loud, and with **as much detail as possible,** an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between **six years and twelve months ago**. I would like you to recall an event or meeting related to a **specific person**.
(*Prompts:* 'An incident which occurred at hospital?', 'An incident involving a neighbour?' 'Involving a friend, a doctor or nurse?')

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

E.4.2. I would like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred between six years and twelve months ago, related to a **trip or journey**. (*Prompts:*'At a place you visited?', 'Involving someone you met?', 'While you were travelling?')

Description / Free Recall:			
	Prompts	**Notes**	**Score**
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how <u>you</u> felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		
		Total Score	

E.4.3. Finally, I would like you to describe out loud, and **with as much detail as possible**, an incident or event *(PAUSE),* that stands out for you *(PAUSE),* that occurred that occurred between six years and twelve months ago. For this memory, I would like it to be related to a **family event**. (*Prompts:* 'An incident involving a relative?', 'Involving a visit somewhere?', 'On a family holiday?'

Description / Free Recall:

	Prompts	Notes	Score
1. Event Detail *Has the free recall covered the prompts? Stop once you have enough to know it was a once-off event*	Was this a once-off event? What happened? Their relationship to you? What was the weather like? What were you wearing? What food / music / transport?		
2. Temporal Specificity *Minimum is first 3. *Otherwise, morning or afternoon?*	What year? What date? What time of day? * What month? What season? What day of the week?		
3. Sensory / Perceptual Detail *The aim is to elicit details. Stop if first 2 questions elicit detail, otherwise continue.*	What can you visualize or picture about that event? What sounds / smells / tastes? Is this memory vivid or vague? What textures / physical sensations?		
4. Spatial Specificity *Stop if first two provided*	Where did this event occur? Where were you within that scene? What country / city / street? What building / floor / room?		
5. Emotion	Can you recall how you felt at the time?		
6. Thoughts	Can you remember what you were thinking, at the time?		
7. Implication *Within the 24 hours prior to, & up to 24 hours after the main event*	What happened beforehand that day? What happened afterwards that day?		**Total Score**

Appendix I: Examples of avoid events sheets for a PD-active group participant interview (upper panel), and a PD-passive group participant (lower panel)

[redacted] *CE2 C2 13.01.17*		*"That's great, but I'd like you to try to think of something else"*	*Used*
A1 E.1.1.		As a toddler at Worcester Street / climbing stairs / parents' reaction	
A2 E.1.2.		Playing near netball courts / chasing game / hurting himself	
A3 E.1.3.	-	Race qualifier for the team that took part in the interschool competition at Rongotai College, Wellington	
	+	**Lancaster Park Rugby Ground / All Blacks match / view obscured**	
A5 E.2.1.	-	(Anything related to wedding at Eliza Manor House)	
	+	**Brother-in-law making a best man speech at his wedding**	
A6 E.2.2.		Watching a running race and standing next to a girl / girl making a comment about her sister / who was taking part in the race	
A4 E.2.3		Working at Stats department / lunch break / playing snooker	
E.3.1.			
E.3.2.			
E.3.3			
A7 E.4.1		Leaving hospital / taking a fall / further damaging his archilles heel	
A9 E.4.2.	-	Trip to salmon farm near Takaka, and catching a fish	
	+	**Trip to UK in 2011 / tour of WWI sites / relative's name on memorial**	
A8 E.4.3.		Avoid anything related to the retirement party	

[redacted] *CE2 C2 21.12.16*		*"That's great, but I'd like you to try to think of something else"*	*Used*
A1 E.1.1.		Walking to kindy / needing the toilet / asking at a house	
A2 E.1.2.		Went to a new school for a few weeks / because mother was having a baby / was cheeky to the teacher	
A3 E.1.3.	-	Forgetting the words to a poem in class / caned by the teacher / put head in locker	
	+	**Ozymandias poem / class-time / the teacher**	
A5 E.2.1.	-	Wilding Park / a bouquet pin up someone's nose / photographer snapped moment	
	+	**After wedding / Penny and the bouquet / the photo**	
A6 E.2.2.		Meeting a man called Roger McDonald / when he began a job / at the airport	
A4 E.2.3		When working as an apprentice / forced to use something / to use an old laithe	
E.3.1.			
E.3.2.			
E.3.3			
A7 E.4.1		Visiting the eye hospital / cause of eye problems / new discovery for doctors	
A9 E.4.2.	-	Visiting the Great War exhibition / during last trip to north Island / at the museum	
	+	**Great War exhibition / Te Papa / personal significance**	
A8 E.4.3.		Great granddaughter coming to visit regularly / Jenny	

Appendix J: Secondary data analysis

The secondary analysis only included memories that were different to those produced at baseline. These memories could be spontaneously provided on the first request by the examiner; or upon request for an alternative memory, if participants had initially produced a baseline memory.

For 23 events, participants failed to recall any memories at all and were awarded zero scores (HC n=5, PD-Intervention n=7, PD-Control n=5). These are marked as '*e*' events in the Results Table 3-2. The data for these events were treated identically in the main analysis reported in the Results chapter.

For an additional 17 events, participants produced a 'baseline memory' but were unable to think of a different memory. These are marked as '*f*' events. These events were also awarded zero scores. The data for these events were included in the main analysis reported in the Results chapter.

There were an additional 17 events affected by administration error in which the baseline memory was spontaneously produced but the participant was *not asked to* think of an alternative event ('f^1' events). Because it was not known whether participants would have been able to produce an alternative memory if they had been asked, these event scores were re-designated as 'missing values'. The mean values of the life periods from whence they came were re-calculated as a percentage of the remaining two events.

Additionally, there were three 'replacement' baseline events that were used, because an elaborated event was spontaneously provided, and the participant could not think of an alternative memory ('*d*' events). These were rescored as zero because they were elicited under conditions where the participant was asked to but had been unable to think of a

different memory. The original scores for these events were included in the main analysis reported in the Results chapter.

PD-active event 2.1. (event '*b*'): This event score was re-designated as a missing value. This is because it was a baseline event used in memory elaboration sessions, and the participant was not asked to think of an alternative memory. This event's Early Adulthood life period score was calculated using the mean percentage score of the two remaining events. This event score was treated identically in the main analysis reported in the Results chapter.

PD-active event 1.3. (event '*a*'): This event was rescored as zero because even though it was an elaborated baseline event, the participant was firstly asked to think of a different memory and could not. Events 1.1, 1.2 for this participant are therefore included for analysis. For the main data analysis reported in the Results chapter, this event was excluded as a 'missing value' and the life period total was calculated from the remaining two event scores.

Appendix K: Autobiographical memory end-of-trial scoring sheet

Table K-1. *Combined EAMI and AMI semantic scoring table used at end-of-trial.*

EAMI	SEMANTIC	AMI	EAMI	AMI
	CHILDHOOD			*Children Part 6*
Age 0 - 5		*Before School Part 1*	S.2.3.1. (1)	
	S.1.1.1. (2)		S.2.3.2. (0.5)	
	S.1.1.2. (3)		S.2.3.3. (0.5)	
	S.1.1.3. (3)		S.2.3.4. (1)	
	S.1.1.4. (1)		S.2.3.5. (0.5)	
	S.1.1.5. (1)		S.2.3.6. (0.5)	
	S.1.1.6. (1)		S.2.4.1. (3)	
	S.1.1.7. (1)		S.2.4.2. (1)	
/ 10		/ 5		/ 4
Age 5 - 11		*First School Part 2*	*/ 14* *TOTAL*	*/ 21*
	S.1.2.1. (1)		**LATER ADULTHOOD Age 45 - 6 yrs ago**	
	S.1.2.2. (1)		S.3.1. (2)	
	S.1.2.3. (1)		S.3.2. (3)	
	S.1.2.4. (2)		S.3.3. (3)	
	S.1.2.5. (1)		S.3.4. (1)	
	S.1.2.6. (3)		S.3.5. (1)	
	S.1.2.7. (3)		S.3.6. (1)	
	S.1.2.8. (1)			
/ 10		/ 8	S.3.7. (1)	
Age 11 - 18		*High School Part 3*	S.3.8. (3)	
	S.1.3.1. (1)		S.3.9. (1)	
	S.1.3.2. (1)		*/ 14* *TOTAL*	*0*
	S.1.3.3. (0.5)		**RECENT LIFE**	
	S.1.3.3.1. (0.5)		*6 yrs - 12 mths ago*	*Present Hospital Part 7*
	(S.1.3.4.) (1)		S.4.1.1. (1)	
	S.1.3.5. (2)		S.4.1.2. (1)	
	S.1.3.6. (1)		S.4.1.3. (1)	
	S.1.3.7. (3)		S.4.1.4. (2)	
	S.1.3.8. (3)		S.4.1.5. (3)	
/ 10		/ 8		/ 8
	S.1.4.1. (3)			*Holiday/Journey Part 10*
	S.1.4.2. (1)		S.4.2.1. (1)	
/ 4			S.4.2.2. (1)	
	TOTAL	*/ 21*	S.4.2.3. (1)	
	EARLY ADULT LIFE			/ 3
Age 18 - 30		*Career Part 4*		*Last Christmas Part 9*
	S.2.1.1. (1)		S.4.3.1. (1)	
	S.2.1.2. (2)		S.4.3.2. (1)	
	(S.2.1.2.1.) (1)			/ 2
	(S.2.1.2.2.) (1)			*Previous Hospital Part 8*
	S.2.1.3. (1)		S.4.4.1. (1)	
	S.2.1.4. (3)		S.4.4.2. (1)	
	S.2.1.5. (3)		S.4.4.3. (1)	
	S.2.1.6. (2)		S.4.4.4. (2)	
	S.2.1.7. (1)		S.4.4.5. (3)	
		/ 8	S.4.4.6. (3)	
		Wedding Part 5	S.4.4.7. (1)	
	S.2.2.1. (1)		S.4.4.8. (1)	
	S.2.2.2. (1)		S.4.4.9. (1)	
	S.2.2.3. (2)		S.4.4.10. (1)	
	S.2.2.4. (2)		S.4.4.11. (3)	
	S.2.2.5. (1)		S.4.4.12. (1)	
	S.2.2.6. (1)			/ 8
	S.2.2.7. (1)		/ 14 *TOTAL*	/ 21
		/ 9	**/ 76 MAX TOTAL**	**/ 63**

Note. Item S.4.4.5. refers to AMI only. Item S.1.3.4. is relevant only to American users of the interview and was not included in any analyses.

Table K-2. *Combined EAMI and AMI episodic scoring table used at end-of-trial.*

EAMI Episodic Event	**Childhood 0–18yrs**			**Early Adulthood 18–30yrs**			**Later Adulthood 45–65yrs ago**			**Recent Life Last 6yrs–12mths ago**		
	0–5	**5–11**	**11–18**									
	E.1.1.	E.1.2.	E.1.3.	E.2.1.	E.2.2.	E.2.3.	E.3.1.	E.3.2.	E.3.3.	E.4.1.	E.4.2.	E.4.3.
Event												
Temporal												
Sensory												
Spatial												
Emotion												
Implication												
Thoughts												
TOTAL /7												
Avoid Event Used												
AMI Episodic Event	**A1**	**A2**	**A3**	**A5**	**A6**	**A4**				**A7**	**A9**	**A8**
	/3	/3	/3	/3	/3	/3				/3	/3	/3
TOTALS /27		/9			/9						/9	

EAMI Autonoetic Consc.	E.1.1.	E.1.2.	E.1.3.	E.2.1.	E.2.2.	E.2.3.	E.3.1.	E.3.2.	E.3.3.	E.4.1.	E.4.2.	E.4.3.
1. Viewer Perspective												
2. Continuity of Visual Imagery												
3. Covert Rehearsal of Memory												
4. Emotional Re-experiencing												
5. Overall Re-experiencing												

Note. The 'EAMI Autonoetic Consciousness'. table was not included in this thesis.